A Dissertation in General Surgery

A COMPARATIVE STUDYBETWEEN APACHE II AND RANSON SCORING SYSTEMS IN PREDICTING THE SEVERITY OF ACUTE PANCREATITIS

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DR. R. SUNDARA PANDIYAN

LIST OF ABBREVATIONS USED

ACCR	-	Amylase Creatinine Clearance Ratio
APACHE II	-	Acute physiology and chronic health evaluation
AUC	-	Area Under Curve
CAPAP	-	Carboxy Peptidase Activation Peptide
CFTR	-	Cystic Fibrosis Transmembrane Regulator
CRAI	-	Continous Regional Arterial Infusion
CRP	-	C-reactive Protein
CTSI	-	Computed Tomography Severity Scoring
IL	-	Interleukin
NFKB	-	Nuclear Factor Kappa B
NPV	-	Negative Predictive Value
PLA2	-	Phospolipase A2
PPV	-	Positive Predictive Value
PSTI	-	Pancreatic Secretory Trypsin Inhibitor
SAPS	-	Simplified Acute Physiology Scoring
TAP	-	Trypsinogen Activated Peptide
TNF	-	Tumor Necrosis Factor

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INTRODUCTION

Acute pancreatitis is a condition which involves a wide variety of clinical signs and symptom. The course of which ranges from a mild self limiting inflammatory process to a more fulminant course which could involve multiorgan dysfunction and lead to mortality.

The crux of the treatment lies in early diagnosis and appropriate management. Acute pancreatitis should be differentiated from other diagnoses and patients should be stratified accordingly and managed appropriately.

There are several scoring systems in predicting the severity of acute pancreatitis of which the commonly used are APACHE II and RANSONS scoring systems. But the usage of these two are still under debate and hence the essential for the study.

OBJECTIVES

To compare the RANSON scoring system with APACHE II in predicting the severity of acute pancreatitis

REVIEW OF LITERATURE

HISTORY

AMBROSE PARE in 1579 gave an early description about acute pancreatitis. But the importance of the pancreas and its implications on the human body systems were not felt at that time. Only it was in the middle of the seventeenth century NICHOLAS SENN indicated that surgical management could be done for pancreatic gangrene and abscess formation.

In 1889, Reginald Fitz suggested early operative intervention was harmful and dangerous, after presenting its classic clinical and pathologic presentation.

In 1901, during the autopsy OPIE found impacted gallstone at ampulla of vater and suggested it could be the cause of acute pancreatitis and death.

The acceptable explanations of acute pancreatitis were given by OPIE,HALSTEAD and OSLER while working at john Hopkins hospital.

SIR BERKELY MOYNIHAN in 1925 quoted that “acute pancreatitis is the most horrible of all the abdominal calamities”.

Acute pancreatitis as a disease or disorder ranges from mild localized inflammation to life threatening multisystem organ failure such as sepsis, renal impairment and acute respiratory distress syndrome and death.

The treatment of acute pancreatitis for decades remained the same in the form of supportive measures instead of treating the root cause that is the culprit organ pancreas. Outcomes are improving now a days due to the efficient scoring systems and advent of the advanced imaging modalities and minimally invasive procedures. The new imaging modalities revolutionized the management of acute pancreatitis and make the correct staging of the disease process such as localized inflammation, necrosis, gangrene formation, pseudocyst formation.

DEFINITIONS

Acute Pancreatitis is an inflammatory process which involves local tissues and more far distant remote tissues which thereby becomes a systemic illness. COMPUTERISED TOMOGRAPHY AND ENDOSCOPIC RETROGRADE CHOLANGIO PANCREATOGRAPHY (ERCP) differentiate the disease process from acute and chronic.

ACUTE PANCREATITIS could be mild or severe

MILD disease does not involve any organ dysfunction where as the severe disease involves multiple organ failure

The approved markers of acute severe pancreatitis are 3 or more of RANSON criteria for non gallstone pancreatitis and 8 or more of the ACUTE PHYSIOLOGY ANC CHRONIC HAELTH EVALUATION .

Contrast enhanced CT scan differentiates the interstitial from necrotizing pancreatitis.

PSEUDOCYST is defined as fluid collection encapsulated by granulation tissue or fibrous wall for 4 to 6 weeks.

PANCREATIC NECROSIS is a diffuse or focal area of inflammation with peripancreatic fat necrosis.

AN ACUTE FLUID COLLECTION in contrast to the pseudocyst is localized collection of fluid which is not walled by granulation tissue or fibrous wall.

NATURAL HISTORY

The natural course of the disease in 80% of the patients are usually mild or self limiting confined to the pancreas and remaining 20% of the patients suffer from extreme severe disease course with the mortality ranging from 2 to 11%.

The disease process is very rapid with bimodal peaking time. Most deaths in united states, about one half in the first week or two.

In latin American nations most deaths occur within 24 hours (25%). One third of the deaths occur within 48 hours.

Young patients with no comorbid illness have better clinical outcome than those with other comorbidities who suffer much from the disease .inflammation and scarring of the pancreatic tissues make the life miserable in patients who survive ths acute episode. Most patients due to the resulting stricture of pancreatic duct develop malabsorption, diabetes mellitus and obstructive pancreatitis.

Patients who are obese develop local complications. Severe acute pancreatitis and acute respiratory distress syndrome more frequently than non obese individuals.

PATHOLOGY

Acinar cell injury particularly peripheral acinar cells which are most vulnerable to the ischemia remains the mainstay in the pathology of acute pancreatitis . other injuries are due to fat necrosis and autodigestion. Infectious agents, toxins are directly noxious to the acinar cells .in contrast to the above ductal necrosis is the earliest lesion produced due to hypotension in pancreatitis.

Pathologically pancreatitis can be divided into necrotizing and interstitial

Interstitial pancreatitis involves edema of the pancreatic acinar cells associated with the inflammatory cells infiltration. Usually interstitial pancreatitis runs a milder course.

Acute necrotising pancreatitis involves pancreatic fat necrosis of larger area involvement and necrosis of larger area which usually has macroscopic and microscopic involvement .severe necrosis usually seen in the periphery of the pancreatic cells but in due course may also involve the major part of the gland. Macrophages and granulocytes demarcate the areas of inflammation from normal areas. Clinically acute necrotizing pancreatitis involves a more severe clinical course and the outcome is usually poor and associated with large scale morbidity.

PATHOGENESIS OF ACUTE PANCREATITIS

Trypsin is the major culprit in the pathogenesis of acute pancreatitis. Normally tryps in is the enzyme which catalyses the conversion of trypsinogen tn trypsin which actively involves the cascade of the reactions which starts the process of

conversion of proenzymes including elastase, phospholipase and carboxypeptidases. The trypsin in excess amounts are usually inactivated and excess trysin if any are inactivated. The inactivation factors such as PANCREATIC SECRETORY TRYPSIN INHIBITOR(PTSI) which inactivates the 20%of the enzyme activity. Mesotrypsin and enzme Y are the other other enzmes trypsin itself acts to inactivate excess trypsin. antiproteases such as ANTITRYPSIN and uz-macroglobulin. other methods of protection of pancreatic cells from injury are intracellular sequestration of trypsin during synthesis and transport and the separation of cathepsin B as they travel through the golgi apparatus .cathepsinB activates the trypsinogen to trypsin. Autoactivation of trypsin are also prevented by low intracellular, intra acinar concentrations of calcium.

Various etiological hypothesis has been postulated for the acute pancreatitis which involves the activation of trypsin and inactivation of the enzyme. COLOCALIZATION of pancreatic enzymes ,which is followed by injury to the acinar cells is a widely accepted hypothesis.

Inhibition of cathepsin B prevents activation of trypsinogen. Colocalization of cathepsin B to the lysosomal enzymes which forms the unstable vacuoles which are easily destabilized leads to cascade of pancreatic inflammatory reaction. Cholecystokinin analogue cerulean prevents the trypsinogen activation by inhibiting the pancreatic cathepsin B which strongly supports the colocalization hypothesis. Acute pancreatitis hence may be treated bycathepsin B inactivation.

Various experimental model suggests that with in 10 minutes the trypsin gets activated and trypsin activation peptide getting accumulated with in the pancreas and leading to pancreatic cell damage and acinar cell necrosis. The cleavage of TAP when trypsinogen gets activated and its concentrations gets constantly elevated in plasma,urine and gets sequestered as ascitic fluid.

MUTATION THEORY

CFTR (cystic fibrosis transmembrane conductance regulator) gene mutations are common in the etiopathogenesis of acute pancreatitis .more than 1200 mutations are there for cftr gene so far in world literature ,the severity of these various mutations ranges from mild to severe and fulminant producing a highly viscus pancreatic juice ,concentrated acid, and pancreatic insufficiency in infancy. These are usually seen In homozygotes, whereas heterozygote mutation cause recurrent pancreatitis by ductal cell dysfunction and alteration of acinar cell function. Bicarbonate conductance gets altered. The normal function of the CFTR channel is to secrete the chloride and bicarbonate anions into the ducts flushing away of the liberated enzymes and proenzymes in to the duodenum.

SPINK 1 is a gene which is protective in function for pancreatic acinar cells. mutations of which causes the damage to the acinar cells. The accurate mechanism is not clear but the mutation of SpINK1 gene could limit the activity of trypsin

PATHOGENESIS OF GALLSTONE PANCREATITIS

Recent passage of gallstone could injure the sphincter of oddi and causes the reflux of bile into the pancreatic duct and cause the gallstone related pancreatitis. Bile reflux secondary to edema or stone at the ampulla of vater when it passes through the common bile duct gets impacted at the ampulla at sphincter of oddi. Inherent incompetence of the sphincter of oddi in addition to the gallstone disease could lead to more severe disease .but the exact mechanism remains unclear .

Mixture of bile juice with pancreatic enymes could lead to the pancreatic acinar cell inflammation due to the excess permeability of the main pancreatic duct. The theory of common channel remains a debate. Normally the intra-pancreatic duct pressure is higher than the pressure in the common bile duct, thereby making the reflux of the bile unlikely. Likewise bile reflux from the duodenum is also unlikely due to the fact that after sphincterotomy or sphincteroplasty by open or endoscopic methods the resultant pancreatitis is unlikely, thereby making the theory of common passage or pathway theory unlikely.

Impacted gallstone at the distal common bile duct which causes the obstruction of the confluence of the ducts causes the acute pancreatitis and this theory is popular and supported by the fact that ligation of the main pancreatic duct causes severe necrotizing pancreatitis and lead to acinar cell damage and this within 3 days if not decompressed lead to progression of acinar cell necrosis and thereby resulting necrotizing pancreatitis which sometimes could be fulminant.

PATHOPHYSIOLOGY

The pathophysiology of acute pancreatitis involves the usual inflammatory cascade and lead to initial acinar cell injury which has to tamed initially, failing which leads to propagated, unchecked responses ranging from local inflammation, later leading to systemic response. Which later lead to release of inflammatory cytokines, super radical induced injury to the ductal and acinar cell epithelium, causing leakage of excessive pancreatic fluid in the loco regional tissues and bacterial translocation to the pancreas and later it enter into the systemic circulation.

Endothelial cell damage lead to the initial injury to the pancreatic ductal and acinar cell which is usually mediated by the VCAM 1(vascular cell adhesion molecule)

The ongoing inflammation and ischemia in the pancreatic tissues sometimes eventually lead to the pseudocyst formation due to the disruption of the pancreatic duct leading to local fluid accumulation within the pancreatic tissues and surrounding it.

Acute pancreatitis due to the microvascular damage not only affects pancreas but also it elicits as the systemic response affecting the lungs, kidney, heart, and numerous metabolic derangements. Pleural effusion, myocardial depression, acute respiratory distress syndrome, systemic inflammatory response syndrome all mediated by the pancreatic enzymes which are activated such as phospholipases, elastases, and mainly by trypsin and inflammatory cytokines such as PAF and TNF

.mediators released from the pancreas to the portal circulation. Once reaching the portal circulation mediators reach the kupffer cells of the liver induce hepatic expression and cytokine expression into the systemic circulation. CRP and IL-6 are the acute phase reactants which are the major culprits which evokes the cell damage in the lungs, heart, kidney and terminates in the multiorgan dysfunction and failure.

Metabolic complications such as hypocalcemia, hyperlipidemia, hyperglycemia sometimes hypoglycemia occurs in acute pancreatitis. ARDS due to the inefficient surfactant production and destruction by the active phopholipase A (lecithinase) which digests it .acute renal failure is attributed to the hypovolemia and hypotension, myocardial depressant factor, a major factor induces myocardial depression and death. The pathogenesis of hypocalcemia is multifactorial and it is explained on the basis of soap formation. Hypomagnesimia, hypoalbuminemia are also attributed to the cause as hypocalcemia.

Hormonal imbalances such as parathormone, calcitonin, and glucagon ,the effects of which binds free calcium by forming fatty acid –albumin complexes, intracellular translocation of calcium and exposure to endotoxin.

Pancreatic infection (pancreatic necrosis / abscess) occur from the translocation of colonic bacteria and from the lymphatics due to the breakage of the protective barrier. Normally there is a protective barrier, so that bacterias cannot translocate to the inflamed areas. Due to the break in the protective mechanisms in pancreatitis the impermeability is insulted. Gut ischemia due to the hypovolemia and AV shunting in the gut causes the penetration of the bacteria through the gut barrier.

CAUSES OF ACUTE PANCREATITIS

Conditions predisposing to acute pancreatitis are listed in the in following table. Hope the list is not exhaustive and will continue to grow. In India alcoholism accounts for 70% of the causes. Gall stone diseases also has the major share in the etiology.

OBSTRUCTIVE CAUSES

Gall Stones

Gallstones are the most common obstructive cause sof acute pancreatitis accounting for about 40% of the cases of it. The incidence of gallstones causing pancreatitis is higher in men than in women . cholecystectomy with CBD exploration reduce the chance of one getting the recurrence of the symptoms and signs of acute pancreatitis. Smaller stones of less than 5mm in diameter are more prone to cause the disease than the stones which are greater than 5mm in diameter as the smaller stones pass easily from the cystic duct to the ampulla.

GALL BLADDER SLUDGE /MICROLITHIASIS

Association of GB sludge and acute pancreatitis is unproved. Sludge contains cholesterol monohydrate crystals and calcium bilirubinate granules. on ultrasonography it appears as the mobile, hypodense particles and it gets layered in the most dependant part of the gall bladder. Usually the patients are asymptomatic. Usually sludge occurs with bile stasis. Ceftriaxone, a cephalosporin antibiotic has

been implicated in the GB sludge formation due the precipitation reaction with bile salts.

Prolonged fasting, distal duct obstruction and total parenteral nutrition are causes implicated.

When the solubility of a substance exceeds in bile, these start to precipitate and result in sludge. The association between the sludge and pancreatitis remain unclear. Cholecystectomy has not been proved yet in curing acute pancreatitis in case of GB sludge.

TUMOURS

Intraductal mucinous tumours of pancreas by obstructing the ductal opening can elicit acute pancreatitis and it is commoner in patients older than 40 years and they are usually recurrent. Large adenomas ,metastatic tumours and adenocarcinomas in a minority of cases also can cause acute pancreatitis.

Duodenal diverticula, choledochoceles, space occupying parasites such as CLONORCHIS and ASCARIAS and annular pancreas also cause the pancreatitis by obstructive means.

Drug induced pancreatits involves several pathogenetic mechanisms, of which hypersensitivity reactions appear to a major factor. The pancreatitis features sets up only after 4 to 6 weeks after initiation of therapy not after the single dose but

in the rechallenge phase it ensues suddenly after taking the drug. Amiinosalicylates ,azathioprine, tetracyclines are the drugs which acts by this mechanism.

Other mechanism by which it causes acute pancreatitis is the accumulation of toxic metabolites due to prolonged exposure to the drug for the months altogether. Examples are didanosine and valproate.

Tamoxifen, thiazides and isotretinoin are the drugs that produce hypertriglyceridemia.

Normally the course of drug induced pancreatitis is mild and self limited.

TOXINS

Smoking causes the risk of acute pancreatitis in alcohol induced and not in gall stone pancreatitis. Hyperstimulation of pancreas by the organophosphorus compounds and the venom of the scorpion of Trinidad also lead to acute pancreatitis. Methyl alcohol is also implicated in the aetiology of acute pancreatitis.

Acute inflammation which has its classical manifestations such as vasodilatation initially followed by vasoconstriction which leads to stasis and due to which causing the increased permeability of the capillary endothelium leading to acinar cell damage and cellular death, due to the progressive ischemia and propagated inflammatory reaction .

Microcirculation gets affected due to the above mentioned responses and added on this a reperfusion injury which is caused by the oxidative cell damage

induced by the free radicals. Though the certainty of the ISCHEMIA-REPERFUSION theory of cell damage is not clear in pancreas, it is widely accepted .

Recruitment of macrophages and granulocytes into the area of inflammation is mediated by complement mediated activation of proinflammatory cytokines. Macrophages and granulocytes release the inflammatory mediators such as INTERLEUKINS, TUMOUR NECROSIS FACTOR, NUCLEAR FACTOR KAPPA, leucocyte adhesion molecule and ICAM 1, VCAM 1, TRANSFORMNG GROWTH FACTOR BETA, IL-6, IL-8, IL-1.

Other mediators of inflammation include arachidonic acid metabolites such as leukotrienes, prostaglandins, platelet activating factor, nitric oxide, reactive oxygen species that overwhelm the scavengers of the antioxidant systems that act endogenously.

Usually these substances act on the pancreatic microcirculation which causes endothelial cell damage and thrombus formation and vascular leakage which leads to haemorrhage and lead to acute haemorrhagic pancreatitis leading to pancreatic necrosis. Acinar cell glutathione concentrations leading to oxidative stress and permanent cell damage.

ALCOHOL DRUGS AND TOXINS

The machanism of alcohol induced pancreatitis is unclear. There are several hypothesi s related to this issue. One such is that the relaxation if sphincter of oddi and thereby reflux of bile into the pancreatic duct and thereby initiates the

inflammatory process.it also increases the synthesis of pancreatic enzymes and lysosomal enzymes of pancreatic acinar cells. Some other hypothesis include increased protein concentrations in accumulated pancreatic juice in long term alcohol consuming persons, which obstructs the small ductules of the pancreatic acinar cells and other theory suggests that alcohol particularly ethanol and one of its metabolite induces a direct injury to the pancreatic acinar cells.

Genetic background is suspected by the fact that all chronic alcohol consumers are not developing chronic pancreatitis. But till date no strong genetic hypothesis has been postulated in this regard.

DRUGS

These are undoubtedly the important cause for acute pancreatitis. But most cases are unconvincing . Drug induced pancreatitis as a diagnoses can be made after ruling out the other possible causes and there should convincingly an appropriate time interval between the initiation of drug consumption and its effect.

Drugs causing hypertriglyceridemia causes acute pancreatitis and noticingly it is produced with rechallenge with the drug. The table in the ensuing page shows the individual specific drug causing acute pancreatitis . most cases are idiosyncratic and a specific drug from the group causes it instead of the whole group.

HEREDITARY AND GENETIC CAUSES

Pancreatitis with hereditary etiology is an autosomal dominant disorder with penetrance as variable and there are various gene mutations in the etiology of acute pancreatitis. Various gene mutations have been implicated in this disease. Mutations of various protein products and enzymes such as trypsinogen and CFTR are the established etiologies in this.

CFTR mutations accounts for 3 to 40% in atleast one allele causes idiopathic pancreatitis or recurrent or acute pancreatitis or acute on chronic pancreatitis and in a similar proportion of patients presents with PANCREAS DIVISUM .most patients with CFTR mutations have sweat chloride values as normal and mucosal potential difference values as normal, the significance of which is unknown. Recently genomic testing of the entire CFTR gene is also available commercially.

Another mutation of very mild importance is the SPINKI mutation. The association is very weak with the acute pancreatitis because of the fact that this mutation is very common in the common population to the extent of about 2%. Also only 0.5% of the carriers experience the disease in their lifetime and the severity of the disease is also very similar to the patients without mutations. Hence the significance is very weak. Mutations ofN34S is ery common.

Commercial kits of SPINKI analysis and CFTR genome and PRSSI are widely available.

Trypsinogen mutations associated with PRSSI are the most common cause of acute pancreatitis and more than 30 such mutations are described so far and the commonly implicated are R122H and N291. Randomized trials so far shoes that out of these 25%of these are N291 and 52% of these mutations are associated with R122H.

TRAUMA

Blunt trauma of the abdomen in the epigastrium and penetrating injury of the abdomen can damage the pancreas and lead to the liberation of enzymes which lead to activation of enzymatic cascade of reactions leading to acute pancreatitis and thereby elevation of serum amylase and injury could also expand to adjacent organs also.

The plan of treatment is usually laparotomy and proceed and before surgery complete evaluation of pancreas is essential as to include pancreatectomy or not in the surgical procedure.

The injury associated could be to the duct also and include duct rupture and increased pancreatic specific lipase and increase in the serum amylase activity

VASCULAR CAUSES

Pancreatitis could also be caused due to the ischemia, which is usually mild but also lead to necrotizing pancreatitis. Ischemia of the pancreatic vessels may be due to atheroembolism, systemic lupus erythematosus or also due to the sudden hypotension and introperative injuries or embolization of fat plaques, usually from the aorta due to the invisibe procedures such as transabdominal angiography.

Other invasive vascular procedures such as arterial embolization through catheter for hepatocellular carcinoma. MARATHON runners who run a longer tracks also develop acute pancreatitis which is explained on the ischaemic basis. Patients undergoing CABG and pericardial tamponade and cardiogenic shock also develop acute pancreatits due to ischemia .

SURGICAL CAUSES

Surgical causes of acute pancreatitis are the most mortal of all the disease as it ranges from 30% to 50%. Most common surgeries that may lead to acute pancreatitis include cardiopulmonary bypass and various intraabdominal and intrathoracic causes and more than 10%follows liver transplantations. More than 30? Of the patients undergoing cardiac surgeries will have hyperamylaesmia and subsequently develop acute necrotizing pancreatitis. Delay in the diagnosis and the mismanagement of hypotension, medicines such as calciumchloride and azathioprine and various infectious agents as mentioned in previous sections.

ENDOSCOPIC RETROGRADE CHOLANGIOPANCRETOGRAPHY

SPHINCTER OF ODDI DYSFUNCTION, difficult cannulation, pancreatic sphincterotomy , dilatation of the biliary balloon , multiple contrast injection into the pancreas , and various patient characteristics such as diabetes mellitus ,female gender, abnormal serum hyperbilirubinemia, prior existing acute pancreatitis, are the various factors implicated in the causative as the post ERCP pancreatitis .

Technical difficulties and various patient factors are the variables associated with post ERCP. About 10%of the patients with diagnostic ERCP and 15% of the patients with therapeutic ERCP. Patients with prior history of post ERCP pancreatitis definitely develop recurrent attack of recurrent pancreatitis.

PANCREAS DIVISUM

PANCREAS DIVISUM, the congenital malformation which is the most common cause of acute as well as recurrent pancreatitis is due to the various hypothetical issues and facts. Pancreatic divisum with normal main or accessory pancreatic ductular systems are the the cause as acute or recurrent pancreatitis is established, based on the various facts.

1) there is a higher frequency of acute or recurrent pancreatitis in patients with pancreatic divisum.

2) placement of the stent or endoscopic sphincterotomy reduces the risk of the acute pancreatitis.

3) patients without stents or prior sphincterotomy are prone for developing recurrent pancreatitis.

SPHINCTER OF ODDI DYSFUNCTION

40 mm of hg or higher as the intra sphincter pressure is the cause of acute severe pancreatitis. Open or endoscopic sphincterotomy as a cause can relive the sphincter of oddi pressure and relieve the acute pancreatitis, which supports the fact that sphincter of oddi dysfunction as the cause.

MISCELLANEOUS CAUSES

1) sulfasalaziline
2) crohn's disease
3) celiac disease.
4) burns
5) smoking.

CLINICAL FEATURES OF ACUTE PANCREATITIS

The clinical signs and other physical findings are relatively not going to guide you for the exact diagnosis as pancreatitis as most of them are similar to that of any other cause of acute abdomen.

HISTORY

Biliary colic is the common presentation of acute pancreatitis. Pain is usually found in the epigastrium or in the left subcostal ragion with radiation to the back .

Pain starts to appear very rapidly and the pain is typically constant and does not vary with the position and radiation to the back is pathognomonic of acute pancreatitis.

Pain relieved on changing the position and getting relieved by simple medications suggests some other diagnosis such as biliary colic or costochondritis or gastritis.

VOMITING AND NAUSEA

Inflammation of the posterior gastric wall causes retching and vomiting. vomiting does not alleviate the pain. Nearly 100 % of the patients with acute pancreatitis develop acute bilious vomiting and nausea.

PHYSICAL EXAMINATION

1) abdominal tenderness
2) abdominal distension due to colonic ileus
3) epigastris pain
4) gastric ileus or small bowel ileus
5) tenderness elicited on gently percussing the upper abdomen

6) tenderness and guarding

7) abdominal rigidity is due to diffuse peritonitis difficult to differentiate it from the perforated viscus

8) bowel sounds are reduced or absent

9) flank ecchymoses (turner's sign)

10) flank ecchymoses (cullen's) sign, due to the extravasation of haemorrhagic pancreatic exudates

11) brawny erythema of the flanks

12) palpable epigastric mass (pseudocyst or large inflammatory mass)

13) tachycardia with HR>100 to 150 Bpm

14) blood pressure may be normal or low due to the third space losses and hypovolemia

15) temperature may be normal or increase to 101 to 103 degree Fahrenheit owing to the inflammatory mediators

16) tachypnea and shallow respirations due to the sub diaphragmatic inflammatory exudates

17) congestive cardiac failure ,pleural effusions

18) atelactasis

19) acute respiratory distress syndrome due to the lecithinase which destroys surfactant

20) aletred sensorium, hallucinations, disorientation, coma

21) electrolyte imbalances, fever, hypoxia. All due to the action of the pancreatic enzymes on the central nervous system

22) icterus in patients with choledocholithiasis

23) edema of the pancreas causing obstructive jaundice.

24) coexisting liver disease also can cause icterus

25) nodular fat necrosis appearing over the buttocks, scalp,trunk

26) alcoholic pancreatitis manifest as xanthomas of tendons,spider angiomas and hepatomegaly

27) hyperlipidaemic pancreatitis lipemia retinalis

28) band keratopathy seen in hypercalcemia

LABARATORY DIAGNOSIS

Non specific markers of inflammation, specific enzymes of pancreas and urine levels of non enzymatic secretions of the pancreas, and various other miscellaneous tests. Serum lipase increased to about 2 to 3 fold in cases of acute pancreatitis.

URINE AND SERUM AMYLASE

Serum amylase as an marker of inflammation and normal secretion by various organs in the human body. Salivary amylase accounts for about 55 % to 60% and the remaining of the amount secreted by the pancreas . this shows that the amylase level elevation is not only confined to pancreas but also the salivary glands. Moreover the enzyme secreted by the pancreas is a ligand termed as the P – isoamylase. However in practice the measurement of this enzyme is rarely employed when compared to serum amylase which is a non specific marker.

Because of its wider availability and economicity serum amylase level is routinely done when compared to the P-ISOAMYLASE. Serum amylase is rapidly increased on acute pancreatitis in the first 24 hours of inflammation and its level normally decreased by 4 to 6 days after inflammation. Clearance of amylase is usually by plasma clearance and only 23% is cleared by renal route. The earliest marker of inflammation in pancreas is by the measurement of serum amylase when compared to the other biochemical markers or radiological evidences or surgery ,which usually takes more time to present with the signs of acute pancreatitis.

The major disadvantage of serum amylase as a marker of acute pancreatitis is its lack of sensitivity and specificity.

In extreme cases of very severe and fulminant pancreatitis where majority of the pancreatic cell death occurred already the serum amylase levels remains normal.

In very milder cases of acute pancreatitis also the serum amylase level does not serves as a marker of the disease .during the cases of acute on chronic pancreatitis also the amylase level is not increased.

Serum amylase level is also not increased or normal in cases of triglyceride induced pancreatitis. In these cases serial measurements of serum amylase levels are very important to make the diagnose.

HYPERAMYLASEMIA

Hyperamylasemia is not specific for acute pancreatitis and more than 50% of the cases of hyperamylasemias are not due to the pancreatic inflammation. Various conditions associated with this are

1) parotitis
2) salpingitis
3) papillary cystadenoma of the ovary
4) benign cyst of the ovary
5) carcinoma of the lung
6) perforated viscus
7) intestinal infarction
8) patients undergoing renal dialysis

9) renal failure also implicated in the cause of acute pancreatitis though the amylase as such is not cleared by kidney per se.

Creatinine clearance does not match or correlate with the elevations of amylase levels.

Linear cause and the effect relationship doesnot exists between the creatinine clearance and the elevation of the serum amylase, because of the fact that majority of the patients with profound renal failure have normal levels of serum amylase.

There is a condition termed MACROAMYLASEMIA. It is a condition in which the serum amylase is bound to a very large protein or an abnormal protein or abnormal immunoglobulin ,the size of which is too large to be filtered by the glomerulus. Macroamylasemia as a condition can cause the complication in the diagnosis of acute pancreatitis.

If the serum amylase level is normal and its urinary value is elevated, the condition called MUNCHAUSEN'S syndrome should be ruled out . it is a syndrome in which the patient mixes the saliva in urine deliberately ,thereby confusing the diagnoses.

ACCR in urine amylase to creatinine clearance ratio is usually increased in cases of acute pancreatitis in about 3% to 7% of the patients. The importance of which lies in just to diagnose and differentiate the macroamylasemia.

The importance of urinary amylase also lies only in the diagnosis of macroamylasemia and nothing else.

Apart from the indirect measurements of macroamylasemia through the urinary amylase and ACCR, macroamylasemia could also be measured directly.

SERUM LIPASE

Serum lipase as a marker of inflammation in acute pancreatitis is claimed to be far more specific than the serum amylase .the specificity of which is 85% to 100 %.the claim of the serum lipase to be the marker of acute pancreatitis is due to the fact LIPASE originates from the pancreas only. Minimal amount of lipase ,though meagre is due to the elevation of gastric lipase.

This specificity is due to the fact that serum amylase is elevated in variety of gynaecologic malignancies, tumours,salivary gland dysfunction and macroamylasemia .serum lipase gets elevated in the first day of the illness and it gets elevated persistently than the serum amylase . variety of the authors have difference of opinion regarding the usage of serum amylase and serum lipase in combination as the diagnostic tool for acute pancreatitis .

Likewise of the serum amylase which gets increased two to three fold increase in pancreatitis, the lipase value also increase 3 fold in cases of pancreatitis and also in chronic renal insufficiency, thereby adding confusion in the usage as a diagnostic tool of acute pancreatitis.

Opinion differs among researchers regarding the usage of lipase alone or combination with serum amylase in the diagnostic kit.

OTHER ENZYMES

1) pancreatic colipase
2) carboxyester lipase
3) elastase
4) carboxypeptidase A
5) trypsin
6) PLAz
7) ribonuclease

These are non specific enzymes and none of them has diagnostic implications in the acute pancreatitis.

ROUTINE BLOOD INVESTIGATIONS

1) alanine aminotransferases
2) aspartate aminotransferases
3) hematocrit
4) white blood cell count
5) serum glucose

6) glucagon

7) serum bilirubin

8) alkaline phophatase

9) serum triglycerde levels

OTHER BLOOD TESTS

1) pancreas associated protein (PAP)

2) pancreas specific protein (PSP)

3) methemalbumin

RADIOLOGIC DIAGNOSIS:

ABDOMINAL PLAIN FILM:

Findings on a plain radiography range from no abnormalities in mild disease to localized ileus of a segment of small intestine ("sentinel loop") or the "colon cutoff sign" in more severe disease and "Renal Halo" sign. In addition, an abdominal plain film helps exclude other causes of abdominal pain, such as obstruction and bowel perforation. Appearance of the hollow GI tract on an abdominal plain radiograph depends on the spread and location of pancreatic exudates. Gastric abnormalities are caused by exudates in the lesser sac, which produces anterior displacement of the stomach with separation of

the contour of the stomach from the transverse colon. Abnormalities of the small intestine, which are due to exudates in proximity to small bowel mesentery, include ileus of one or more loops of jejunum (the sentinel loop), of the distal ileum or caecum, or of the duodenum. Generalized ileus may occur in severe disease.

Other abnormalities of the hollow GI tract may also be present. The descending duodenum may be displaced and stretched by an enlarged head of the pancreas. In addition, spread of exudates to specific areas of the colon may produce spasm of that part of the colon and either no air distal to the spasm (the colon cutoff sign) or dilated colon proximal to the spasm. Head- predominant pancreatitis predisposes to spread of exudates to the proximal transverse colon, producing colonic spasm and a dilated as ascending colon. Uniform pancreatic inflammation predisposes spread of exudates to the inferior border of the transverse colon and an irregular haustral pattern. Exudates from the

Other findings on plain radiography of the abdomen may give clues to etiology or severity, including calcified gallstones (gallstone pancreatitis), pancreatic stones or calcification (chronic pancreatitis with a bout of acute inflammation), and ascites (severe pancreatitis). Gas in the retroperitoneum may suggest a pancreatic abscess.

CHEST RADIOGRAPHY:

Abnormalities visible on the chest radiographs occur in 30%of patients with acute pancreatitis. They include elevation of a hemidiaphragm, pleural effusions, basal or plate- like atelectasis secondary to limited respiratory excursion, and pulmonary infiltrates. Pleural effusions may be bilateral or confined to the left side; rarely they are only on the right side. During the first 7 to 10 days, there also may be signs of congestive heart failure or ARDS. Pericardial effusion is rare.

ABDOMINAL ULTRASONOGRAPHY:

Abdominal ultrasonography is used during the first 24 hours of hospitalization to search for gallstones, dilatation of the common bile duct due to choledocholithiasis, and ascites. If the pancreas is seen (bowel gas obscures the pancreas 25% to 35% of the time), it is usually diffusely enlarged and hypoechoic. Less commonly there are focal hypoechoic areas. Evidence of chronic pancreatitis, such as intraductual or parenchymal calcification and dilation of the pancreatic duct, may also be seen. Ultra-sonography is not a good imaging modality to evaluate extra pancreatic spread of pancreatic inflammation or necrosis within the pancreas and consequently is not useful to ascertain severity of pancreatitis. During the course of acute pancreatitis, this modality can be used to evaluate progression of a pseudocyst.

Because of overlying gas, evidence of cholelithiasis may be obscured during the acute attack but may be found after bowel gas has receeded.

ENDOSCOPIC ULTRASONOGRAPHY:

Usually, endoscopic ultrasonography (EUS) is not helpful in acute pancreatitis. However, it is more sensitive than either abdominal ultrasonography or CT to detect common duct stones. One potential use of EUS is to exclude a common duct stone in patients with severe pancreatitis and jaundice (serum bilirubin> 5mg/dL), ERCP, in this situation, may worsen pancreatitis and potentially introduce infection into necrotic areas of the pancreas. Thus, EUS might eliminate the need for urgent ERCP in severe gallstone pancreatitis.

COMPUTED TOMOGRAPHY:

CT scan is the most important imaging modality for the diagnosis of acute Pancreatitis and its intra- abdominal complications. The three main indications for a CT scan in acute pancreatitis are (1) to exclude other serious intra- abdominal conditions, such as mesenteric infarction or a perforated ulcer, (2) to stage the severity of acute pancreatitis, and (3) to determine whether complications are present, such as involvement of the GI tract or nearby blood vessels and organs, including liver, spleen, and kidney. Helical CT is the most common technique.

If possible, CT scanning should be performed after the patient receives an oral contrast agent followed by an intravenous contrast agent to identify any areas of pancreatic necrosis. If there is normal perfusion of the pancreas, interstitial pancreatitis is said to be present pancreatic necrosis (perfusion defects after intra venous contrast agent

is given) may not appear until 48 to 72 hours after onset of acute pancreatitis. CT – or Ultrasound- guided needle aspiration can confirm suspected infections.

Contraindications for using intravenous contrast agent are a patient's history of prior sever allergy (respiratory distress or anaphylaxis) and significant renal impairment (serum creatinine >2mg/dL). If severe renal impairment requires dialysis, intravenous contrast medium may be used. Hives or less sever allergic reactions with previous administration of iodinated contrast material are not contraindications. In a patient with such a history, however, a nonionic contrast agent should be used; also, glucocorticoids and diphenhydramine (Benadryl) should be administered before scanning.

Iodinated contrast medium given at the onset of pancreatitis increases necrosis in experimental acute pancreatitis in rats, but not in opossums. Data in humans are conflicting. Two retrospective studies suggested that early contrast-enhanced CT worsened pancreatitis, but this suggestion was not corroborated by a third retrospective study. The severity of acute pancreatitis has been classified into five grades (A to E) on the basis of findings on unenhanced CT. Grade E pancreatitis represents the most severe disease. At least one half of patients with grade E pancreatitis have necrotizing pancreatitis. The majority of patients with pancreatic infection have grade E pancreatitis.

This classification has been further refined into a CT severity index (CTSI) score (Table 4). The higher the CTSI score, the more severe the pancreatitis clinically. Although the presence of gas in the pancreas suggest pancreatic infection with a gas- forming organism, this findings can also accompany sterile necrosis with microperforation of the gut or adjacent pseudocyst into the pancreas. In the great majority of pancreatic infections, however, CT scanning shows no gas.

Table 4: computed tomography (CT) Grading System of Balthazar and CT severity Index scoring System (CTSI) [79]

Balthazar grades	
Grade A	Normal pancreas consistent with mild pancreatitis
Grade B	Focal or diffuse enlargement of the gland, including contour irregularities and inhomogeneous attenuation but without peri pancreatic inflammation
Grade C	Abnormalities seen in grade B plus peri pancreatic inflammation
Grade D	Grade plus associated single fluid collection
Grade E	Grade C plus tow or more peri-pancreatic fluid collections or gas in the pancreas or retroperitoneum
CTSI = Balthazar Grade Score Plus Necrosis Score*	
Balthazar Grade Score: A=0 B=1 C=2 D=3 E=4	
Necrosis score: Absence of necrosis= 0 Necrosis of up to 1/3rd of pancreas =2, Necrosis of ½ of pancreas = 4 Necrosis of > ½ =6	

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) provides information regarding the severity of pancreatitis similar to that given by CT. MRI is as good as CT in detecting necrosis and fluid collections and is a better method to detect choledocholithiasis and ductal disruption, especially after intravenous secretion is administered. Gadolinium, unlike

intravenous contrast agents used for CT, is safe to use in renal failure. MRI, however, is less accessible and more expensive than CT.

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATICO GRAPHY

ERCP is limited to patients with severe acute pancreatitis due to gallstones with persistent common bile duct obstruction as well as to those in whom the stone could not be removed during surgery.

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DIFFERENTIAL DIAGNOSIS:

The differential diagnosis of acute pancreatitis include a variety of conditions associated with severe upper abdominal pain (Table 5). However, the history and physical findings aid in differential diagnosis. The abdominal pain of biliary colic may simulate that of acute pancreatitis; it is frequently severe and epigastric but lasts for several hours rather than several days. The pain of a perforated ulcer is sudden, becomes diffuse, and precipitates a rigid abdomen; movement aggravates pain. Nausea or infarction, the clinical setting often is an older person with cardiac arrhythmia or arteriosclerotic disease who experiences sudden pain out of proportion to physical findings, bloody diarrhea, nausea, and vomiting. Abdominal tenderness may be mild to moderate, and muscular rigidity may not be pronounced despite severe pain. In intestinal obstruction, pain is cyclical, abdominal distention is prominent, vomiting persists and may become feculent, and peristalsis is hyperactive and often audible.

Table 5 Differential Diagnosis of Acute Pancreatitis

Biliary pain/acute cholecystitis
Perforated hollow viscus
Mesenteric ischemia or infarction
Closed- loop intestinal obstruction
Inferior wall myocardial infarction
Dissecting aortic aneurysm
Ruptured ectopic pregnancy

DISTINGUISHING ALCOHOLIC FROM GALLSTONE PANCREATITIS

Differentiation between alcoholic and gallstone pancreatitis is important because eliminating these causes may prevent further attacks. Alcoholic pancreatitis occurs more frequently in men approximately 40 years old. The first clinical episode usually occurs after 5 to 10 years of heavy alcohol consumption. By contrast, biliary pancreatitis is more common in women, and the first clinical episode is often after age 40 years. Recurrent attacks of acute pancreatitis suggest an alcoholic etiology, but unrecognized gallstones may cause recurrent pancreatitis. Among patients with acute biliary pancreatitis who are discharged from hospital without undergoing cholecystectomy, 30% to 50% have recurrent acute pancreatitis a mean of 108 days after discharge. Thus, removing the gallbladder in biliary pancreatitis is imperative.

Laboratory tests may help distinguish between these two disorders. A serum alanine aminotransferase (ALT) concentration above 150 IU/L (approximately a threefold elevation) is 96% specific for gallstone pancreatitis, with a positive predictive value of 95%; however, the sensitivity is only 48%. The aspartate aminotransferase

(AST) concentration is nearly as useful as the ALT concentration, but the total bilirubin and alkaline phosphatase concentrations are not as helpful to distinguish gallstone pancreatitis from pancreatitis of other causes. There are differing reports as to whether a high serum lipase – to- amylase ratio can differentiate alcoholic pancreatitis from pancreatitis of other causes.

Conventional abdominal ultrasonography should be performed in every patient with a first attack of acute pancreatitis to search for gallstones in the gallbladder, common duct stones, and signs of extrahepatic biliary tract obstruction. However, common bile duct stones are frequently missed by this modality, and most stones pass during the acute attack. ERCP is limited to patients with severe acute pancreatitis due to gallstones with persistent common bile duct obstruction as well as to those in whom the stone could not be removed during surgery. The common bile duct can be imaged in most patients with biliary pancreatitis by means of an operative cholangiogram performed at the time of laparoscopic cholecystectomy. Although EUS is the most accurate method of detecting common duct stones and has been recommended for evaluating the common duct prior to cholecystectomy, it is rarely needed in this setting.

Magnetic resonance cholangiopancreatography (MRCP) is another noninvasive modality hat is highly accurate in determing whether common duct stones are present. If a common duct stone is found at surgery, it is removed either at operation or endoscopically after surgery. Laparoscopic exploration of the common bile duct is as safe and effective as postoperative ERCP for cleaning stones from the common duct.

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PREDICTORS OF SEVERITY:

Predicting severity of pancreatitis early in the course of disease is critical to maximize therapy and to prevent and minimize organ dysfunction and complications. Clinical assessment, multiple prognostic scoring lists (Ranson's, Glasgow/Imrie Coma scales, APACHE II), peritoneal fluid analysis, organ failure scores, individual laboratory tests, and CT scanning have all been touted as helpful for this purpose.

SCORING SYSTEMS:

Clinical signs:

Clinical evidence of severe pancreatitis includes signs of peritonitis, shock, and respiratory distress. At 48 hours after admission (the height of their accuracy), sensitivity of these signs is less than 40%, but specificity exceeds 95%. The positive predictive value ranges from 65% to 100%, and the negative predictive value from 74% to 87%.

RANSON'S CRITERIA (TABLE 6)

Table 6 Ranson's 11 Prognostic Criteria for Pancreatitis

Parameter	1974 Criteria for Nongallstone Pancreatitis	1982 Criteria for Gallstone Pancreatitis
At admission		
Age (years)	>55	>70
White blood cell count (cells/ mm^3)	>16.000	>18,000
Blood glucose (mg/dL)	>200	>220
Lactate dehydrogenase (IU/L)	>350	>400
Aspartate aminotransferase (U/l)	>250	>250
During initial 48 Hours		
Decrease in hematocrit (%)	>10	>10
Increase in blood urea nitrogen (mg/dL)	>5	>2
	<8	<8
Calcium (mg/dL)	<60	NA
pO2, (mm Hg)	>4	>5
Base deficit (mEq/L)	>6	>4
Estimated fluid sequestration (L)		

Data from Ranson JHC, Rifkind KM, Roses DF, et al: Prognostic signs and the role of operative management in acute pancreatitis. Surg Gynecol Obstet 139:69, 1974; and Ranson JHC Etiological and prognosis factors in human acute pancreatitis: A review.Am J Gastroenterol 77: 633, 1982. NA, not applicable.

Ranson and colleagues identified 11 criteria that had prognostic significance during the first 48 hours of pancreatitis. The original list was analyzed in patients who primarily suffered from alcoholic pancreatitis and was modified 8 years later for those with gallstone pancreatitis (see Table 2). Higher Ranson's score predicts more

severedisease. In mild pancreatitis (score ≤2) the mortality is 2.5%, and in severe pancreatitis (score 2:3) the mortality is 62%. Also the higher the Ranson's score, the higher the incidence of systemic complications, necrosis, and infected necrosis. These criteriacontinue to remain in wide use in both the United states and Europe.

The Ranson criteria have several drawbacks. First, the two lists are cumbersome Second, an accurate Ranson's score takes 48 hours to compute, and the criteria have not been validated beyond the 48 – hours time limit. Third, not all laboratories measure all the parameters in routine blood tests (e.g., lactic dehydrogenase). Fourth, the overall sensitivity of the Ranson criteria (using 3 signs, as, the cutoff) for diagnosing severe disease is only 40%to 88% and the specificity 43% to 90%. The positive predictive alue is approximately 50% and the negative predictive value around 90%. Therefore, the best use of Ranson's criteria is to exclude severe disease.[78, 79, 82]

THE APACHE SYSTEM:

Acute physiology score and chronic health evaluation.

The first major attempt at a system to quantify severity of illness in ICU patients was the APACHE system, by Knaus et al in 1981.

APACHE I

In the original form, APACHE contained 34 physiologic measurements and included many continuous variables. A value of 0 to 4 was assigned to each variable, according to its degree of abnormality. Shortly after its introduction apache 1 system was disfavoured, because of practical problems like collection of large number of variables. Also under the rules of APACHE system any unmeasured variable was

assumed to be normal and weighted as zero. This gave rise to questions about the models general applicability. Another major criticism of original APACHE system was that the variables were chosen by a group of physicians and hence there was a potential of bias. These inaccuracies in the original APACHE system prevented its widespread use. However, it did serve as a prototype for the development of two subsequent systems.

SAPS

The simplified acute physiology score was developed from APACHE I system and incorporated 13 variables that had the most discriminate power and were the most, frequently measured variables to cover all major organ systems. SAPS score is – still used but has essentially been replaced by APACHE II in many centres.

APACHE II

Published in 1985 by the same author this is the second version of the APACHE system and it contains refinements based on experience with the original APACHE system. APACHE II has been extensively used and has received far more attention in the literature then any of the other methodologies for ICU outcome prediction. It contains 12 continuous variables from the original APACHE system and also takes into account age of the patient, pre- morbid conditions and Glasgow coma scale.

DEVELOPMENT OF APACHE II

Using clinical judgement and documented physiologic relationships to choose variable and assign weights remains the essence of APACHE II. The number of variable were reduced from 14 to 12. Infrequently measured variables such as serum

osmolality, lactic acid level, skin testing for anergy were deleted. Serum BUN was replaced by more specific serum creatinine and serum pH was retained in preference to bicarbonate. Many variables crucial in patient care, such as serum glucose, albumin, CVP and urinary output were found to have less explanatory power. Most of these variables were sensitive to variations in therapeutic decisions than severity of disease.

Some of the thresholds and weights for the physiologic variables have been changed ego Glasgow coma score, serum creatinine. Also since Alveolar – arterial O2 gradient (p [A-a] O2 is heavily dependent on inspired O2 (F1O2) a direct weighting was given to all paO2 values when F1O2 is less than 0.5

To eliminate the problem of missing values and concerns about the assumption that an unmeasured variable was normal, measurement of all 12 variables was made mandatory for usage of APACHE II. The recorded values of the variables are based on the most deranged values during the past 24 hours.

Because age and severe chronic health problems reflect diminished physiologic reserve, they have been directly incorporated into APACHE II. Also, emergency surgery and non operative patients with severe chronic organ system dysfunction were given additional five additional five points in comparison to elective surgical patients who were given only two points because patients with severe chronic conditions are not considered to be candidates for elective surgery.

The maximum possible APACHE II score is 71. In the experience of the author of APACHE II no patient had exceeded 55.The strengths of APACHE II system are:

i) It has a well defined outcome (hospital death)

ii) It was derived from a large database (5815 patients from 13 hospitals)

Short comings of APACHE II system:

Because of extensive usage, important sources of error and bias in the APACHE II system were revealed. First, APACHE II performs well overall in several ICU population but it is inaccurate when looking at specific disease categories because the data base from which it was derived, through large, did not contain many patients in major disease subsets such as cardiac surgery, oncology etc. Second APACHE II does not account for prior treatment or clinical course before the patient enters ICU, this has been labeled as lead time bias. Third, APACHE II requires determination of a single admission diagnosis, a subjective process prone to bias. Finally, despite the reduction in number of variables, measurement error from bedside data collection are still on issue.

APACHE II has been recently refined into APACHE 0, where 0 represents obesity, and this is a better predictor of prognosis than APACHE II. Another modification of APACHE II is the APACHE III system which is now being applied widely to acute pancreatitis clinical trials.

APACHE II has the advantage of being able to be used on a daily basis and its positive and negative predictive values are similar to those of the Ranson score at 48 hours after admission. The Apache II system assigns points for 12 physiologic variables,for age, and for chronic health status, in generating a total point score. The 12 physiologic variables are temperature, heart rate, respiration rate, mean arterial blood

pressure, oxygenation, arterial pH, serum potassium, sodium and creatinine values, hematocrit, white blood cell count, and Glasgow Coma Scale. APACHE II scores on admission and within48 hours help distinguish mild from severe pancreatitis and to predict death. Most patients whose APACHE II scores are 9 or less during the first 48 hours survive. However, patients with APACHE II scores of 13 or more have a high likelihood of dying. At admission, sensitivity of the APACHE II score is 34% to 70%, and specificity is 76% to 98%. At 48 hours, sensitivity remains less than 50%, but specificity is close to 90% to 100%. Strong drawbacks of the APACHE II score are its complexity, its low sensitivity on admission, and the fact that at 48 hours it is no better than other scoring systems. Like the Ranson criteria, the APACHE II score has its highest value in predicting mild disease.

Table 7: Acute Physiology and Chronic Health Evaluation (APACHE)- II Scoring

System of Disease Severity

A. Physiologic variable temperature
Mean arterial pressure (mm Hg)
Heart rate
Respirations
Arterial pH
PaO_2 (mm Hg)
Serum sodium
Serum potassium
Serum bicarbonate (mmol/L) Serum creatinine (mg/dl) Hematocrit (%)
White blood cell count
Glasgow Coma Score
B. **Age Points**
C. Chronic Health Points
APACHE II score = A+B+C

Glasgow Score

The Glasgow score is a slightly simplified list (8criteria) that is used commonly in the United Kingdom. Its drawbacks are similar to those of the Ranson score. Other investigators evaluated organ dysfunction risk factors in a qualitative way and found that the presence of one risk factor predicted serious complications and more than 50 % mortality.

Table 8: Modified Glasgow Criteria: Within 48 Hours of Admission

Criteria	Value
Age (yr)	>55
WBC count (x 100/mm^2)	>15
Glucose (mg/dl)	>180
BUN (mg/dl)	>45
LDH (IU/1)	>600
Albumin (g/dl)	<3.3
PaO2 (mm Hg)	<60
Calcium (mg/dl)	<8

Organ Failure Scores:

Organ failure precedes death in the great majority of patients with acute pancreatitis. The Atlanta criteria (Table 1) define severe disease and enumerate various organs that are susceptible to failure but make no distinction between single- and multiple organ failure or between transient and persistent organ failure. The Atlanta criteria thus cannot be used to prognosticate. Multiple- organ failure or organ failure that is persistent should render a patient more susceptible to death than single- organ or transient organ failure. Therefore, criteria that attempt to qualitatively or quantitatively score organ failure might be more predictive of a fatal outcome than other parameters. The Goris score assigns an organ failure value of 0, 1 or 2 or each of seven main Organ system (respiratory, renal, cardiovascular, hepatic, central nervous, hematopoietic, and GI). A score of 14 is the maximum and indicates severe disease in all systems. A study from Scotland demonstrated that the Goris score was more predictive of death than the Glasgow/Imrie score. In this study of 279 patients with acute pancreatitis, there were no deaths in 189 patients with a Goris score of 0, 7 deaths (9%) in the 75 patients with

a Goris score of 1 to 4, and 10 deaths (67%) in the 15 patients with a score higher than 5. Greater use of organ failure scores are likely to improve prognostication in acute pancreatitis.

PERITONEAL LAVAGE

Percutaneous recovery of any volume of peritoneal fluid with a dark color or recovery of at least 20mL of free intraperitoneal fluid of dark color portends a significant mortality. The sensitivity of peritoneal lavage is 36% to 72%, and the specificity is greater than 80% to 100%. An advantage is that peritoneal lavage can be used any time,but it has not gained wide acceptance because it is invasive.

LABORATORY MARKERS:

The extent of elevation of serum amylase concentration does not distinguish mild from severe pancreatitis. Admission or 24 – hour hematocrit levels may be helpful in distinguishing severe disease, as may the CRP value. Although not generally available clinically, measurements of IL- 6, polymorph nuclear leukocyte, TAP,

serum amyloid A, and procalcitonin may prove valuable because their concentrations in blood or urine may serve to separate mild from severe acute pancreatitis.

Hematocrit value:

A high hematocrit value on admission or failure of a high value to diminish after 24 hours of rehydration is believed to be a sing of hemoconcentration due to etroperitoneal fluid loss and thus a marker of severe disease. One study showed that a hematocrit higher than 44% had a sensitivity of 72% on admission and of 94% after 24hours for detection of organ failure. The negative predictive value at 24 hours was 96%. Study from Germany found no correlation between admission Hematocrit value and organ failure.

C-Reactive Protein: Measurement of CRP, an acute – phase reactant produced by the liver, is used extensively in Europe as a marker of severe pancreatitis. CRP is inexpensive to measure and readily available. The sensitivity for detecting severe disease is 60% to 100% (with cutoffs of 100-210mg/L), and the specificity is 75% to 100^%.

Interleukin – 6: IL 6 is an acute- phase reactant cytokine that is produced by a variety of cells and induces hepatic synthesis of CRP. Several studies have shown that it is a reasonably good marker to differentiate mild from severe pancreatic disease.

Polymorphonuclear leukocyte Elastase: Polymorphonuclear leukocyte elastase rises very early (before CRP) in acute pancreatitis. High levels have been reported to differentiate severe from mild disease, but the test is not generally available.

Phospholipse A2: PLAz is involved in the synthesis of prostaglandins and degrades surfactant in the lung. It may play a role in the pulmonary dysfunction associated with acute pancreatitis. Levels of catalytic type II PLAz have been reported to differentiate between mild and severe disease within 24 hours of admission.

Urinary Trypsinogen activation peptide

TAP is the aminoterminal peptide cleaved from trypsinogen during activation of trypsin, providing a rationale for its use as a marker of acute pancreatitis. It can be measured in plasma, ascites fluid, and urine. The urinary TAP level appears to be the most useful and, if measured within 24 hours of onset of symptoms, distinguishes mild from severe pancreatitis. The sensitivity, specificity, and positive and negative predictive values of TAP measurement for distinguishing sever from mild acute pancreatitis at 214 hours compare favorably with those for CRP value and APACHE II, Ranson, and Glasgow scores.

A serum and urinary carboxypeptidase activation peptide (CAPAP) assay has also been shown to predict early severe acute pancreatitis.

Serum Amyloid A: Serum amyloid A is another early acute- phase reactant that is synthesized in the liver and is associated with the extent of tissue inflammation. Two studies have demonstrated that the level of this serum protein can differentiate mild from severe disease.

Procalcitonin The pro peptide procalcitonin is another acute- phase reactant that has been shown to differentiate mild from severe acute pancreatitis within the first 24, hours after symptom onset. A serum strip test has been developed for this measurement that has a sensitivity of 86% and a specificity of 95% in detecting organ failure.

COMPUTED TOMOGRAPHY

CT scanning has been used to assess severity of pancreatitis. The finding of extensive fluid collections or extensive necrosis has been correlated with severe disease.

In an early study, Balthazar and colleagues LIS showed that death occurred in 5 of 37 (13.5%) patients who had grade D or grade E findings on CT (table 5), as opposed to a of 51 who had grades A through C findings. When assessed with CTSI score (see Table 5),3 of 77 patients (3.8%) with scores of a through 6 died, as opposed to 2 of 11 (18%) with scores 7 through 10. The CT grading scores correlate better with local complications (pseudo cysts and abscesses) than with mortality. Among the 37 patients with grade D or E findings, 54% had a local complication, whereas only 2 of 51 (3.9%) with grades A through C experienced this problem. Thus, the data do not confirm that the CTSI is any more predictive than the grade A-E score. There is controversy in the literature as to whether the extent of necrosis on CT predicts organ failure. Two studies did not find any correlation between these two events. In a third study, however, there was a strong correlation.

CHEST RADIOGRAPHY

A pleural effusion documented within 72 hours of admission by either chest Radiograph or CT scan correlates with severe disease.

TREATMENT

GENERAL CONSIDERATIONS

The patient with acute pancreatitis requires aggressive intravenous hydration and adequate analgesia to eliminate or markedly reduce pain. An order for no oral intake (NPO) is usually in force until nausea and vomiting have subsided. Abdominal pain is treated with analgesics, given parenterally every 3 hours. Morphine can also be used. Dosing is monitored carefully and adjusted daily according to ongoing needs. Although morphine has been reported to increase sphincter of Oddi tone and to raise serum amylase levels, its use to treat the pain of pancreatitis has not been shown to adversely affect outcome. Nasogastric intubation is not used routinely because it is not beneficial in mild pancreatitis. This modality is used only to treat gastric or intestinal ileus or intractable nausea and vomiting. Similarly, proton pump inhibitors and histamine Hz receptor blocking agents are not beneficial and are not used.

Each patient should be carefully monitored for any signs of early organ failure such as hypotension and pulmonary or renal insufficiency via close following of vital sings and urinary output. Rapid respiratory rate should not be assumed to be due to abdominal pain, and blood gas measurements and oxygen supplementation are mandatory in this situation. In cannot be overly emphasized that any patient who exhibits signs of early organ dysfunction should be immediately transferred to intensive care monitoring because deterioration can be rapid and fatal. This may be one of the most important decisions the clinician must make.

FLUID RESUSCITATION

Maintaining adequate intravascular volume in severe disease may require 5 to 10 liters of fluid (e.g., isotonic saline) daily for the first several days. A Swan- Ganz catheter is useful to gauge fluid resuscitation and to avoid fluid overload and congestive heart failure. It is also helpful when cardiovascular status is unstable or respiratory function deteriorates. Aggressive fluid replacement may not prevent pancreatic necrosis. Experimentally, hemodilution to a hematocrit value of around 30% with dextran 60 solution improved the pancreatic microcirculation and oxygenation. When the hematocrit decreased to around 259%, packed red blood cells should be infused to Maintain a hematocrit close to 30%.

RESPIRATORY CARE:

Hypoxemia (oxygen saturation < 90%) requires oxygen, ideally administered via nasal prongs or face mask if needed. If nasally administered oxygen fails to correct hypoxemia or if the patient has fatigue and borderline respiratory reserve, endotracheal intubation and assisted ventilation are required early. It is important to use a Swan – Ganz catheter to determine whether hypoxemia is due to congestive heart failure (increased pulmonary artery wedge" pressure) or is a primary pulmonary problem (normal or low pulmonary artery wedge pressure). ARDS is the most serious respiratory complication of acute pancreatitis because it is associated with severe dyspnoea, progressive hypoxemia,and higher mortality. It generally occurs between the second and seventh days of illness,although it can be present on admission, and consists of increased alveolar capillary permeability causing interstitial edema. Chest radiography

CARDIOVASCULAR CARE

Cardiac complications of severe acute pancreatitis include congestive heart failure, myocardial infarction, cardiac arrhythmia, and cardiogenic shock. An increase in cardiac index and a decrease in total peripheral resistance may be present; they respond to infusion of crystalloids. If hypotension persists even with appropriate fluid resuscitation,intravenous dopamine may help maintain the systemic blood pressure. Unlike other vasoconstrictors, dopamine does not impair the microcirculation of the pancreas.

METABOLIC COMPLICATIONS:

Hyperglycemia may manifest during the first several days of severe pancreatitis but usually normalizes as the inflammatory process subsides. Blood sugar levels Fluctuate widely, and insulin should be administered cautiously.

Hypocalcemia due to low serum albumin concentration causes no symptoms and requires no specific therapy. However, reduced serum ionized calcium may cause neuromuscular irritability. If the patient also has hypomagnesemia, magnesium replacement should restore serum calcium level to normal. Causes of magnesium depletion include vomiting, loss of magnesium in urine, and deposition of magnesium in areas of fat necrosis. When serum magnesium concentration is normal, hypercalcemia with signs or symptoms of neuromuscular irritability requires intravenous administration of calcium gluconate if the serum potassium level is normal and the patient is not receiving digitalis. Intravenous calcium increases calcium binding to myocardial receptors, displacing potassium and possibly inducing a serious arrhythmia

ANTIBIOTICS64

Antibiotics are not needed in mild pancreatitis. However, pancreatic infection (infected necrosis and, less so, abscess) and nonpancreatic sepsis (line sepsis, urosepsis or pneumonia) are major sources of morbidity and mortality in severe acute pancreatitis.Thus, it would seem logical to consider antibiotic prophylaxis to improve the outcome.In the 1970s, controlled studies compared intravenous antibiotics with no therapy in the treatment of mild acute alcoholic pancreatitis. These studies showed no effect of antibiotics on the illness. However, low- risk patients were studies (mild alcoholic disease with no mortality) and what later proved to be the wrong antibiotic (ampicillin) was used.In the 1980s, the bacteriology of infected pancreatic tissue was elucidated through analysis of either surgical specimens or fine needle aspirates of the pancreas. These studies showed that the majority of organisms discovered were gram-negative aerobic or anaerobic species (E. coli, Enterobacter aerogenes, Pseudomonas aeruginosa, Proteus species, Klebsiella pneumonia, Citrobacter freundii, Bacteriodes species), with occasional

gram- positive species (Streptococcus fecalis, Staphylococcus aureus, Streptococcus viridians, Staphylococcus epidermidis) and rare fungi (Candida species).Studies in the early 1990s elucidated the antibiotics most appropriate for addressing these organisms and taking into account the level of penetration of antibiotics into necrotic pancreatic tissue. Imipenem, fluoroquinolones (ciprofloxacin, ofloxacin, pefloxacin), and metronidazole emerged as the drugs that achieved the highest inhibitory concentrations in pancreatic tissue, unlike amino glycosides

study added oral nonabsorbable antibiotics to the intravenous antibiotic brew. Although several of these studies found reductions in the rates of pancreatic and nonpancreatic infection with antibiotic therapy, only one reported an improvement in survival However, two meta – analyses of the intravenous antibiotic trial showed that mortality of necrotizing pancreatitis was significantly reduced by antibiotics. Very little comparative data are available as to which antibiotic is the most effective. One study comparing pefloxacin with imipenem in severe disease showed the latter to be significantly more effective in reducing pancreatic and extra pancreatic infection, but mortality was unaffected. Likewise, little information is available on the duration of treatment. One investigation compared 1 week with 3 weeks of ciprofloxacin and found that longer Treatment reduced the rates of pancreatic and non pancreatic infections.

The aforementioned studies have been criticized because they were not placebocontrolled double- blind studies. Furthermore, the use of prophylactic antibiotics in all patients with severe pancreatitis raises the concern that some patients might become superinfected with drug resistant organisms or fungi, leading to great mortality in the future. One double- blind, controlled study randomly assigned 114 patients with severe acute pancreatitis to receive either prophylactic ciprofloxacin plus metronidazole or placebo. Patients in whom infection was suspected were given open- lable antibiotics.There were no differences in rates of infected necrosis or mortality in the two groups.The only difference in rates of infected necrosis or mortality in the two groups. The only difference noted was that 46% of those assigned to placebo eventually received openlabel antibiotics, compared with only 28% of those receiving ciprofloxacin.practice guidelines published before this 2004 study had recommended.

the use of prophylactic antibiotics in patients with servere necotizing pancreatitis. However, given this latest information, another reasonable approach would be to withhold antibiotics pending signs of infection.

Table 9: Prospective, Randomized Prophylactic Antibiotic Trials in Acute Pancreatitis

Authors, Year	No. Antibotics/Control	No. Institutions	Antibiotics	Outcomes	Strengths/Weaknesses
Isennianri et at 2004	58/56	19	Ciprofloxacin, metronidazole	No difference in pancreatic infections or morality	Prospective, randomized, adequately powered
Luiten et al 1995	52/50	16	Cefotaxime, colistin, amphotericin B, norfloxacin	Decreased local infections and mortality	Utilized selective digestive decontamination
Sainio et al 1995	30/30	1	Cefuroxime	No different in pancreatic infections, sepsis; decreased mortality	Underpowered, single center
Pederzoli et al 1993	33/41	6	Imipenem	Decreased local infections and sepsis; no difference in mortality	Unblended, underpowered, subgroup analysis

ENDOSCOPIC THERAPY

Urgent Removal of gallstones in gallstone pancreatitis

Early removal of a possibly impacted gallstone to improve the outcome of gallstone pancreatitis remains a controversial issue. There have been three randomized,fully published studies comparing urgent ERCP and sphincterotomy (for any retained stone) with conventional treatment in the management of gallstone pancreatitis. The earliest study, a single- center investigation from England found, that urgent ERCP performed within 72 hours of admission improved the outcome (complications and mortality) of patients with severe but not mild, acute gallstone pancreatitis. A single center study from Hong Kong, found that the group in whom urgent ERCP was performed had lower rates of biliary sepsis and showed a trend toward lower morality than the control group. The third and largest study, from Germany, involved 22 centers and found a higher complication rate and worsened mortality trend in the urgently treated

ERCP group than in the group undergoing standard nonurgent therapy. Differences in the designs of these studies do not allow direct comparisons. It can be said, however, that there is consensus that severe acute gallstone pancreatitis with ascending cholangitis (jaundice and fever) is an indication for urgent ERCP. However, f severe pancreatitis is unaccompanied by cholangitis, results of the German study would suggest withholding ERCP, whereas those of the English study would suggest proceeding with urgent early ERCP.

Endoscopic Therapy of Pancreatic Duct Rupture

Pancreatic ductal rupture leading to peri pancreatic fluid collections is common in necrotizing pancreatitis. In a prospective ERCP study of biliary pancreatitis, Uomo and colleagues SO noted a 30.5% rate of main pancreatic duct leakage. It has been proposed that early endoscopic stenting of the main pancreatic duct in patients with this problem may shorten hospital stay and reduce the need for subsequent necrosectomy. No controlled studies have yet been reported, and there is the theoretical concern that stenting may cause infection of a sterile fluid collection.

NUTRITIONAL THERAPY

Mild pancreatitis does not require special nutritional feedings. Intravenous hydration is continued until the patient no longer has significant abdominal pain, nausea,or vomiting. Oral feedings can then be initiated. The question as to which factors can predict which patients will show poor response to refeeding was addressed by one study. One hundred sixteen patients with acute pancreatitis were fed at the clinician's discretion.

Twenty-one percent of patients has pain on refeeding of 250 kcal/day. Those who did so nearly doubled ' their stay in the hospital (33vs. 18 days) compared with those in whom pain did not reappear. A prefeeding serum lipase level more than three- fold higher than normal doubled the risk of a pain relapse with refeeding (39%, versus 16% in those with normal serum lipase). However, most patients with lipase values that high prior to refeeding did not have pain with refeeding. These observational data are insufficient to guide clinicians as to when to start refeeding. Serum lipase can remain elevated for long periods after pancreatitis, and it seems reasonable to feed the

no or very few calories when pain and nausea have subsided without regard to the enzyme levels. The diet can then be advanced slowly as tolerated.In patients with more severe pancreatitis, total parenteral nutrition (TPN) initially has appeal because it allows the pancreas to remain completely at rest while the patient's nutritional needs are met, But comparisons between TPN and either intravenous peripheral nutrition or enteral nutrition have shown that TPN is more expensive and carries a higher complication rate. Sax and associates randomly assigned 54 patients with mild pancreatitis to either intravenous nutrition of TPN. The latter group had a higher number of septic complications and a longer hospitalization.

McClave and coworkers randomly assigned 30, patients with mild or moderate pancreatitis to TPN "or" enteral feedings administered through a nasoenteric tube beginning 48 hours after admission. The Ranson and APACHE II scores and glucose Levels normalized more quickly in the enteral group, and the length of hospitalization in That group showed a trend toward a shorter stay. Windor and colleagues randomly assigned 34 patients as follows; those with mild/moderate pancreatitis to either oral feedings or TPN, and those with severe pancreatitis to either enteral feedings via a nasoenteric tube or TPN. The group receiving oral/enteral feedings has shorter ICU stays and showed improvements in acute- phase response markers and disease severity scores compared with the TPN group, finally, Kalfarentzos and associates randomly assigned 38 patients with sever necrotizing pancreatitis to either TPN or nasoenteric feedings. The enteral nutrition group had fewer septic complications and fewer total complications, although duration of hospital stay, duration of ICU stay, and days until resumption of regular diet were the same in the two groups.

Thus these studies demonstrate that enteral nutrition is cheaper and safer and is preferable in patients with severe acute pancreatitis. When nutrition should be initiated and for how long it must be continued, however, are still not established. Furthermore it is unclear whether nasoenteric feedings are needed or whether nasogastric or even oral feedings are similarly effective if the patient tolerates this modality. Along those lines, a UK group randomly assigned 50 patients with severe pancreatitis to either nasogastric or nasoenteric tube feedings. No difference between the groups was seen in the ability to tolerate feedings, in markers of inflammation, or in morbidity or mortality.

SURGERY

The role of the surgeon is primarily two- fold in pancreatitis, to remove the gallbladder in cases of gallstone pancreatitis and to debride pancreatic necrosis or drain a pancreatic abscess if these complications develop. A consensus conference of surgical guidelines suggested in 2002 that in mild and severe gallstone pancreatitis, cholecystectomy should be performed as soon as the patient has recovered and the inflammatory process has subsided, with regard to pancreatic necrosectomy, the data are more complicated. Studies in the 1980s suggested improved mortality with early necrosecfomy (within the first week of hospitalization for severe disease). However, in the only randomized study comparing early (within 72 hours of admission) with late (>12 days after admission) necrosectomy, the mortality was higher after early operation than after later debridement (56% vs. 27%).Some investigators have reported that it is important to, differentiate sterile necrosis from infected necrosis via fine-needle aspiration of the pancreas. Sterile

necrosis scan be managed nonoperativley, because the mortality rate of this condition Without surgery is less than 5%. Infected necrosis (as documented by fine- needle Aspiration of the pancreas), however, is widely regarded as an indication for immediate Surgical debridement because of the belief that infected necrosis treated medically has a nearly uniform fatal outcome. On the other hand, surgical therapy of infected pancreatic necrosis carried a substantial mortality rate, 15% to 73%. This fact has led to the recommendation that patients who are into showing improvement with maximal medical therapy or who show new signs of organ failure should undergo fine needle aspiration of the pancreas.The finding of infection should then lead to immediate surgical intervention. One surgical team, however, had demonstrated that the timing of surgery, not the bacteriologic status of the pancreas, determines surgical mortality. This group operated a mean of 31 days after onset of illness (considerably later than most groups) and documented only a 6.2% surgical mortality with no difference in mortality

patients with sterile and infected necrosis; these results are corroborated by another surgical team who compared early necrosectomy (a mean of 5.6 days after symptoms) with late necrosectomy (mean of 16.6 days after symptoms). Earlier operation was associated with a much higher mortality than delayed surgery (42% vs. 14%) whether infected or sterile necrosis was present. These studies suggest that delaying operation to allow for the acute inflammatory process to subside improves mortality whether or not Infection is present.The natural history of infected necrosis remains largely unknown because of the prevailing propensity for clinicians to operate immediately or to use other

drainage on documentation of such infection. In small case series and one larger series, however, survival has been achieved with antibiotic therapy alone. Fine needle aspiration in these series led to appropriate changes of antibiotics. No controlled studies in this area have been performed. Clearly, the management of infected necrosis requires further definition by studies the elucidate its natural history. Necrosectomy also appears to have deleterious effects on long-term exocrine and endocrine function of the pancreas compared with no necrosectomy. Thus, if at all possible, surgical necrosectomy for sterile or infected necrosis should be avoided unless the patient does not experience improvement. If intervention is needed, delaying until the fourth week or later is advisable. Drainage of a pancreatic abscesses by surgical, radiologic, or occasionally, endoscopic approaches are advised. Unlike pancreatic infected necrosis, a pancreatic abscess is a poorly marginated collection of pus near the pancreas that appears on CT scanning as a low density mass that may contain air bubbles. The cause may be

Secondary liquefaction and secondary infection of an area of necrosis or infection of a pancreatic pseudocyst. Most pancreatic abscesses occur later than infected necrosis, at least 4 weeks after the onset of acute pancreatitis. In general, the mortality of a pancreatic abscess is less than that of infected necrosis.

OTHER APPROACHES OF QUESTIONABLE EFFICACY

Pancreatic protease inhibitors have been used to treat established severe acute pancreatitis and to prevent post ERCP pancreatitis. Gabexate mesylate is the most widely studied pancreatic protease inhibitor. A meta- analysis of five clinical trials of gabexate mesylate in acute pancreatitis found no effect on the 90- day mortality rate but a lower incidence of complications. Multiple trials of somatostatin or its synthetic analog,

Octreotide, have failed to show convincing evidence of efficacy in the treatment of acute pancreatitis. The use of anti- inflammatory cytokines has so far not been beneficial. The largest experience has been with lexipafant, a PAF inhibitor, after initial promising reports, subsequent studies have not shown clear efficacy.Japanese investigators have suggested that, pancreatic protease inhibitors and antibiotics can be better targeted to the affected regions in the pancreas with continuous regional arterial infusion (CRAI) into the celiac, splenic, inferior pancreaticoduodenal,and common hepatic arteries. Using CT, Anai and colleagues showed that with CRAI,the contrast material was distributed to the entire pancreas in six of nine patients with inflammation of the entire pancreas; in the remaining three patients, contrast material did not penetrate the entire area of pancreatic inflammation. Two later studies suggested that intra- arterial infusion of protease inhibitor (nafamostat mesylate) plus imipenem reduces mortality compared with intravenous infusion of the same agents. These studies warrant

further investigations.

In randomized studies, many other measures have been ineffective, including Anticholinergics, glucagon, fresh frozen plasma, and peritoneal lavage.

COMPLICATIONS:

The complications of acute pancreatitis can be divided into local complications Secondary to the inflammatory process in the retroperitoneum and systemic complications,(table 10).

Table 10: complications of acute pancreatitis

Local

Sterile necrosis

Infected necrosis

Abscess

Pseudocyst

Gastrointestinal bleeding:

Pancreatitis- related:

Splenic artery rupture or splenic artery pseudoaneurysm rupture

Splenic vein rupture

Portal vein rupture

Splenic vein thrombosis leading to gastroesophageal varies with rupture

Pseudocyst or abscess hemorrhage

Postnecrosectomy bleeding

Non- pancreatitis – related:

Mallory- Weiss tear

Alcoholic gastropathy

Stress- related mucosal gastropathy

Splenic injury:

Infarction

Rupture

Hematoma

Fistulization or obstruction of small or large bowerl

Right- sided hydronephrosis

Systemic

Respiratory failure

Renal failure

Shock (circulatory failure)

Hyperglycemia

Hypocalcemia

Disseminated intravascular coagulation

Subcutaneous nodules due to fat necrosis

Retinopathy

Psychosis

LOCAL COMPLICATIONS

PANCREATIC NECROSIS

In about 20% of patients with acute pancreatitis, CT shows necrosis. Pancreatic Infection is uncommon in interstitial pancreatitis but may occur in 20% to 50% of Patients with necrotizing pancreatitis. Infection typically appears within the first 2 weeks of illness. In comparison, as mentioned previously pancreatic abscess due to acute pancreatitis does not usually occur until after the first month of illness.

PANCREATIC PSEUDOCYST

A pseudocyst may occur secondary to acute pancreatitis, pancreatic trauma, or chronic pancreatitis. It usually contains a high concentration of pancreatic enzymes and varying amounts of tissue debris. Most pseudo cysts are sterile.

Regardless of size, an asymptomatic pseudocyst does not require treatment. It is Satisfactory to monitor the pseudocyst with abdominal ultrasonography every 3 to 6 months. In two studies, there were no deaths among patients treated either medically or Surgically.Pseudocysts can be complicated by infection, intracystic hemorrhage, or rupture leading to pancreatic ascites. Further, pseudocysts can migrate into the chest or other unusual locations. In patients with known pseudocysts, new symptoms, such as abdominal pain, chills, and fever, should alert the clinician to the emergence of an Infected pseudocyst or abscess. Treatment choices include surgical, radiologic, and endoscopic drainage. No randomized prospective trials have compared these methods. Surgical drainage of a pseudo cyst is possible with a cystogastrostomy or

Cystduodenostomy if the pseudo cyst wall is broadly adherent to the stomach or duodenum. Other procedures are a Roux-en-Y cystojejunostomy and pancreatic Resection if the pseudo cyst is in the tail. Surgical mortality is 6% or less. Pseudocyst Recurrence after internal drainage occurs in 15% of cases and is more common if the main pancreatic duct is obstructed down stream from the surgical anastomosis. For this reason, a prebperative ERCP is usually performed to determine whether there is duct obstruction. In the presence of duct obstruction, a resection of the pseudocyst is preferred.Percutaneous catheter drainage is effective treatment to drain and close both Sterile and infected pseudocysts. As with surgical drainage, percutaneous catheter drainage may fail if there is obstruction of the main pancreatic duct downstream from the pseudocyst. Therefore, an ERCP is usually performed before catheter drainage is attempted.

Two endoscopic methods to decompress a pancreatic pseudocyst are (1) an Endoscopic cyst- gastrostomy or cyst- duodenostomy and (2) insertion of a stent through the ampulla directly into the pancreatic duct and then into the pseudocyst itself. The former method is possible if the pseudocyst is broadly adherent to the wall of the stomach or duodenum. The endoscopist then inserts a double – pigtail stent through the hollow viscus into the cyst. Some endoscopists also insert a transpapillary pancreatic duct stent into the cyst. This is possible if ERCP shows continuity between the pseudocyst and the main pancreatic duct with either method, the catheter is removed after 3 to 4 weeks if closure of the pseudocyst is seen on CT. In failure of radiologic or endoscopic drainage of a pancreatic pseudocyst increases morbidity.

And prologns hospitalization. There are several complications of endoscopic drainage of peseudocysts. The most important is

Bleeding; the risk of bleeding may be reduced if endoscopic ultrasonography is used to be certain that there are no large vessels in the drainage aorta. Infection may occur if the

double pigtail catheter becomes occluded. Use of a nasocystic drain to irrigate the cyst may prevent this complication, An endiscopically placed stent in the pancreatic duct may induce ductal changes identical to those of chronic pancreatitis; for this reason, a stent should be removed after several weeks. If a pseudocyst accompanies considerable pancreatic necrosis, endoscopic and percutaneous catheter drainage should be used very cautiously, because neither technique can evacuate the underlying particulate necrotic marerial, even though both are successful in eliminating the fluid of the pseudocyst itself. In this situation, surgical drainage may be preferred because necrotic debris can be retrieved before the cyst enteric anastomosis.

GASTROINTESTINAL BLEEDING:

GI bleeding may arise from effects not related to the local inflammatory aspects Of pancreatitis, such as stress induced mucosal gastropathy, Mallory- Weiss tear, and Alcoholic gastropathy. Alternatively, bleeding can be due to the inflammatory aspects of The pancreatitis- believed to occur from the irritative effects of liberated activated enzymes on vascular structures or pressure necrosis of inflammatory debris or fluid collections on surrounding structures. Rupture of the splenic artery, splenic vein, or Portal veins have been reported. High mortality is reported with these complications. Temporizing treatments with interventional radiologic techniques are employed, followed by more definitive surgical ligation and resection.

Acute and chronic inflammatory processes of the pancreas can cause thrombosis Of the adjacent splenic vein, which can lead to gastric varices with or without esophageal varices. The varices can rupture, yielding massive bleeding. This problem can be treated via endoscopy with banding of varices or splenectomy, the latter of which is curative.Pseudocysts can be complicated by pseudo aneurysm formation, which can usually be seen by dynamic contrast- enhanced CT. If the pseudo aneurysms bleed, arteriography with embolization is the treatment of choice. Rarely, bleeding into the pancreatic duct occurs (hemosuccus pancreaticus), although it usually occurs in chronic pancratitis.Postnecrosectomy bleeding is common and can be caused by overly aggressive debridement or the placement or use of noncompliant drainage tubes next to vascular structures.

SPLENIC COMPLICATIONS

Splenic complications of acute pancreatitis include intra splenic pseudo cysts, Infarction and necrosis of the spleen, splenic rupture, and hematoma. Some of these Complications can be life- threatening and require emergency splenectomy.

INTESTINAL COMPLICATIONS

Pressure necrosis from inflammatory debris from the tail of the pancreas can obstruct or perforate the bowel or can fistulize into the small or large intestine. The most common site is – the left colon. Treatment is frequently surgical.

SYSTEMIC COMPLICATIONS:

Organ Dysfunction

Respiratory insufficiency is the most common systemic complication associated with pancreatitis. The causes are multifactorial and include pleural effusions, pneumonia, atelectasis, and ARDS. Oxygen supplementation, antibiotics, pleurocentesis, and assisted ventilation may be necessary. Renal complications ae due to hypovolemia causing prerenal azotemia or hypotension leading, to acute tubular necrosis. These are treated with an increase in intravenous fluid administration for the case or hemofiltration or hemodialysis for the latter. Shock is usually caused by hypovolemia secondary to third space losses, vomiting, and interstitial visceral edema. Other uncommon sources are myocardial infarction and pericardial effusions. Fluid replacement it severe acute pancreatitis is best accomplished via central venous monitoring. As mentioned previously, mortality is substantially raised with increasing organ dysfunction, especially if shock is involved.

Metabolic disturbances

Hyperglycemia and hypocalcaemia are common in severe disease. hyperglycemia Usually transient, is due to insulin deficiency from presumed islet cell necrosis hyper Glucagonemia. It is uncommon for these complications to require aggressive treatment.

Fat necrosis

Fat necrosis occurs in subcutaneous tissue, bone, retroperitoneal tissue, Peritoneum, mediastinum, pleura and pericardium, fat cells are necrotic and are Associated with a diffuse inflammatory infiltration. The subcutaneous lesions are

Circumscribed, tender, red nodules that are adherent to the skin but are movable over Deeper structures. Most commonly they occur over the ankles, figures, knees, and elbows. The lesions may drain. Through the skin, rarely, there is also necrosis of adjacent tendons or involvement of joints, particularly the metatarsal, interphalangeal, wrist, knee, and ankle joints. The lesions usually resolve after days to weeks.

Coagulation Disorders: Mild predisseminated intravascular coagulation defects are Common in acute pancreatitis as measured by D-dimer levels in the blood. Full- blown Disseminated intravascular coagulation with a bleeding diathesis associated with a Hypercoagulable state is very uncommon.

MISCELLANEOUS COMPLICATIONS

Pancreatic encephalopathy consists of a variety of central nervous system Symptoms occurring in acute pancreatitis, including agitation, hallucinations, confusion, Disorientation, and coma. A similar syndrome may be due to alcohol withdrawal, and other causes are possible, such as electrolyte disturbances (e.g, hyponatremia) and hypoxia. Purtscher's retinopathy (discrete flame: shaped hemorrhages with cotton-wool spots) can cause sudden blindness; its believed to be due to microembolization in the choroid and retinal arteries.

METHODOLOGY

The present study is a prospective study of 50 cases of Acute pancreatitis admitted in Royapettah Hospital, Kilpauk medical college Chennai, during the study period from May 2014 to august 2014.fifty cases for the purpose of the study were selected on the basis of the nonprobability (purposive) sampling method.

Source of study:

All patients diagnosed with acute pancreatitis admitted in Govt. Royapettah Hospital, Kilpauk Medical College, Chennai 10.

Inclusion criteria:

All patients diagnosed with acute pancreatitis based on the clinical suspicion and elevated serum amylase.

Exclusioncriteria:

- Hyperamylasaemia due to other causes
- Chronic pancreatitis
- Acute on chronic pancreatitis
- Previously diagnosed case of acute pancreatitis

Method of collection of data:

All patients diagnosed with acute pancreatitis based on the clinical suspicion and increased serum amylase levels admitted in govt .royapetteh hospital are assessed with multiple clinical and laboratory variables of both Ranson and Apache II scoring system and the final score of the patient from both the scoring systems are assessed to know their efficacy in predicting the severity of the disease (higher the score more severe the disease).

STATISTICAL METHODS APPLIED:

Data was analysed statistically using WILCOXON SIGN RANK TEST and FISHERS EXACT TEST by SPSS version 17.

$P<0.05$ was considered to be significant.

OBSERVATION AND RESULTS

A total of 50 patients were included in the study .All had an admitting diagnosis of acute pancreatitis .All 50 patients fulfilled the inclusion criteria:

- Clinical suspicion of pancreatitis
- Increased amylase
- Features of Pancreatitis on USG ABDOMEN

Of the 50 patients ,age range was 24-60years (mean-42years), 29 (58%)were men and 21(42%) women. The causes of acute pancreatitis included biliarystone 22(44%),alcoholism 16(32%),idiopathic12(24%).10(20%)patients were chronic smokers and 13(26%) had atleast one co-morbid disease. The common concomitant diseases were hypertension (37.5%), diabetes mellitus(25%) ,ischaemic heart disease(5%).

Overall,12(24%)patients suffered from severe pancreatitis and 38(76%) had mild acute pancreatitis of which all 12 had severe attack as per APACHE II score(>8) and only 4 of these were considered severe by RANSON score(>3) .The systemic complications were multiorgan failure in 3(6%) ,respiratory2(4%) and renal 2(4%) all seen in patients with severe score as per APACHEII .No death occurred and mortality was nil .Local complications occurred in 3 patients (6%) and both had acute fluid collection .All the complications were seen in patients with severe score as per APACHE II and none as per RANSON score.

RANSON Scores:

Table11: Ranson scoring system results

Score	Frequency	Percentage
<3	46	92%
3– 4	4	8%
5-6	Nil	-
>6	Nil	-
TOTAL	50	100%

(Score>3 suggests severe pancreatitis)

In our study only 4 patients had score more than 3, suggesting that only 8% of them were considered to be having severe pancreatitis as per Ransons criteria.

APACHEII Scores:

Table12: Apache II scoring system results :

Score	Frequency	Percentage
0-5	36	72%
6– 10	7	14%
11–15	4	8%
>15	3	6%
TOTAL	50	100%

(Score>8 suggest severe pancreatitis)

In our study 12 patients were diagnosed to have score more than 8 of the 50 cases, suggesting that 24% had severe pancreatitis as per Apache II scoring criteria.

Data was analysed using Wilcoxon sign rank test & Fishers exact test .The value at cutoff point was expressed as sensitivity, specificity, ppv, npv & area under the ROC curve**. P<0.05 was considered to be significant.**

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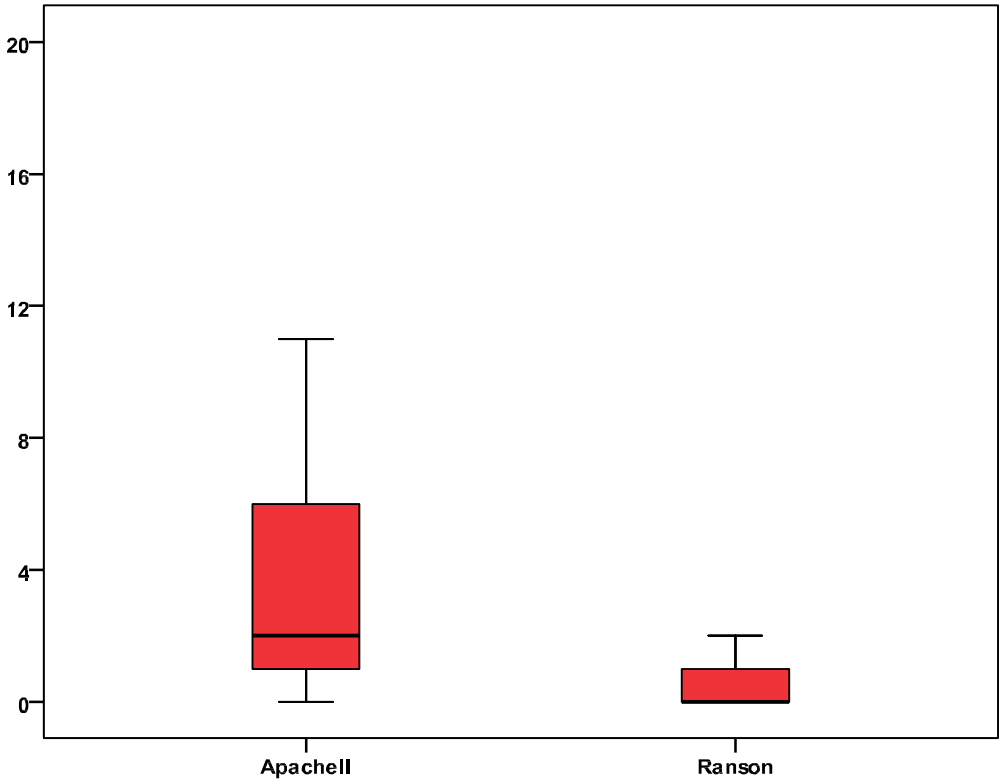
Table 13: Analysed data of Ranson and ApacheII scores:

Severityofacute PancreatitisScore	Median	Interquartile Range	Z	P
ApacheII	2	7	4.491	<0.0005
Ranson	0	1		



Graph:1

Table 14: Ranson – patient frequency

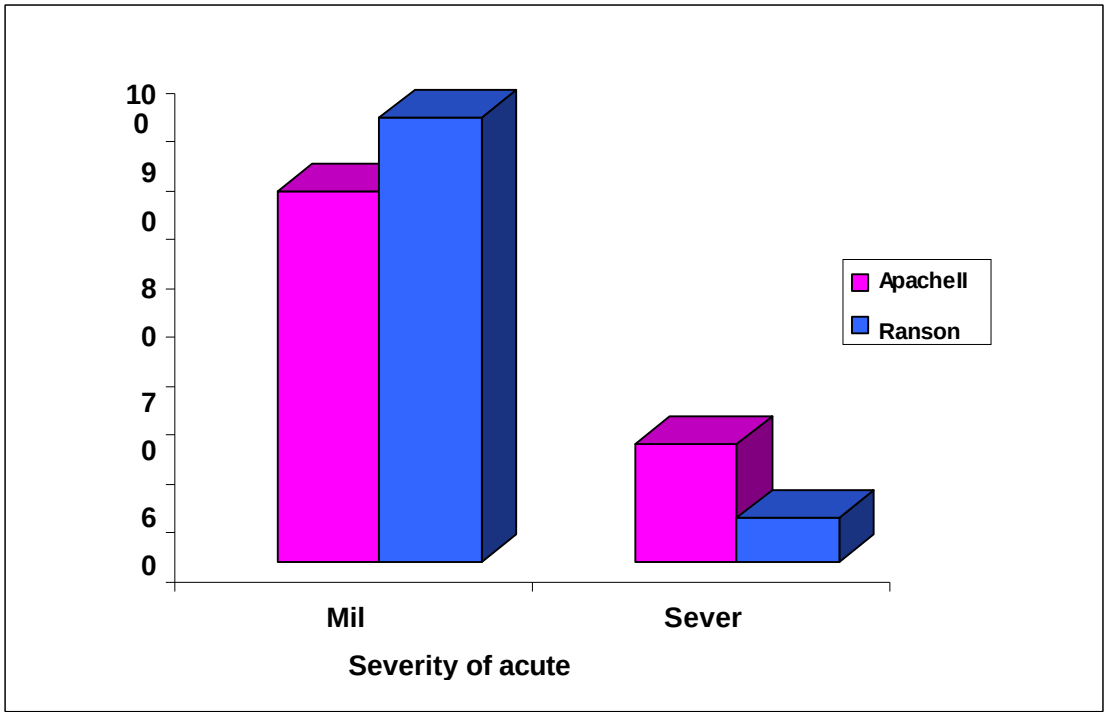
		Frequency	Percent
Valid	Mild	46	92
	Severe	4	8
	Total	50	100

Table 15: Apache II – patient frequency

		Frequency	Percent
Valid	Mild	38	76
	Severe	12	24
	Total	50	100

Table 16: Percentage table (both scoring system together)

		Ranson		Total
		Mild	Severge	
Apache Mild	Count	38	0	38
	% of Total	76%	.0%	76%
Severe	Count	8	4	12
		16%	8%	24%
Total	Count	46	4	50%
	% of Total	92%	8%	100.0%



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(Percentage of mild and severe pancreatitis)

APACHE II

Table17: Predictive performance: Area under curve =0.717

		a Apache b		
		Mild	**Severe**	Total
Serum amylase	Positive Count	8	12	20
	% within Apache	20.0%	100.0%	40%
	Negative Count	30.4%	0	30
	% within Apache	80.0%	.0%	60%
Total	Count	38	12	50
	% within Apache	100.0%	100.0%	100.0%

P<0.0005

Sensitivity = 100%

Specificity = 80%

ppv = 62%

npv = 100%

Ranson

Table18:Predictive performance:- Area under curve = 0.667

		Ranson		Total
		Mild	**Severe**	
Serum amylase	Positive Count	1	3	4
	% within Ranson	25%	75%	8%
	Negative Count	45	1	46
	% within Ranson	86.7%	25%	92%
Total Count		46	3	50
	% within Ranson	100.0%	100.0%	100.0%

P<0.0005

Sensitivity=66.7%

Specificity=86.7%

Ppv=33%

Npv=96%

DISCUSSION

Severe acute pancreatitis usually declares itself shortly after the onset of symptoms and delayed progression from mild to severe disease is uncommon[9]. Assessment of the severity of acute pancreatitis is important for early identification of patients who may benefit from additional supportive and specific therapeutic procedures .It is also important tto standardize clinical data for comparision of results between centres[1,10]. Ideal predicting criteria should therefore be simple, non-invasive, accurate and quantitative, and the assessment tests should be readily available at the time of diagnosis .Amongst the multi-factorial scoring systems, Ranson system is classical though the ApacheII system appears to provide the best accuracy.

This study has demonstrated that the Apache II scoring system is better than the Ranson system in predicting the severity of acute pancreatitis. The AUC of Apache II score was 0.717 and that of Ranson was 0.667, Sensitivity of Apache II was 100% and that of Ranson 66.7%, Specificity of Apache II was 80% and Ranson 86.7%, ppv of ApacheII 62% and Ranson 33%, npv of ApacheII 100% and Rason 96% respectively.

The incidence of acute severe pancreatitis in this study was 24% (12cases), Apache II score showed 76% mild (38cases) &24% (12cases) severe pancreatitis and Ranson score showed 8% (46cases) mild & 92% (4cases) severe. These results were probably due to Apache II system having more number of variables and also incudes the chronic health status of the patient than the Ranson scoring system resulting in Apache II being more accurate in predicting the severity of pancreatitis.

In a study done by Yeung YP[6], the results are follows. It is compared with present study.[82]

Table19: Comparison of AGE in present study with standard literature

AGE (years)	Present study (33cases)	Yeung.Y. pstudy (101cases)
Mean Age in years	42years	68years
Range	24-60years	20-96years

Table20: Comparison of the SEX in present study with standard literature

SEX	Present Study	Yeung.Y.Pstudy
Male	29 (58%)	43 (42.6%)
Female	21 (42%)	58 (57.4%)

TABLE 21: COMPARISON OF THE CAUSATIVE FACTORS

CAUSE	Present Study	Yeung.Y.P study
Biliarystones	22(44%)	59(58.4%)
Alcohol	16(32%)	3(3.0%)
Idiopathic	12(24%)	23(22.8%)
Otherfactors	Nil	16(15.8%)

In this study ,acute pancreatitis was found more commonly in males than females; male:female ratio being 58%:42% and mean age was 42 years. These results can be compared to the Savio GBarreto and JudeRodrigues study where the male female ratio was 96.1%:3.9% and mean age was 40 years ,by Kimmo I.Halonena et al it was 83.7:16.3 and mean age was 43.62 yrs indicating increased incidence in males and also the 4th decade of life being most frequent incidence of age group[71,72].

In the present study alcohol was the etiological factor in 32% of patients and gallstones in 44% compared to alcohol l being 92.6% and gallstones 19% in Savio G Barreto and Jude Rodrigues study and in KimmoI . alcohol accounted to 79.1% and gallstones to 13.2% showing that alcoholism most frequently the etiological factor.[71,72]

Of the 50 patients, 38(76%) had mild disease while 12(24%) had severe Disease (based on Atlanta Criteria for Severe Acute Pancreatitis; APACHEI Iscore >8 was considered severe, and RANSON score>3 was severe). In Savio G Barreto and Jude Rodrigues study 67% had mild disease while 33% patients had severe disease .74.07% had mild disease and 25.93% had severe disease in AbbasiJ. Akhtar et al study[73,71].

The overall mortality rate was nil as compared to Savio GBarreto and Jude Rodrigues study where the overall moratlity was 12% and 14% in AbbasiJ. Akhtar et al study[73,71].

Comparing outcomes in patient groups based on a range of APACHEII scores, it was observed that complications like acute fluid collection, major organ failure were more common when APACHEII scores exceeded 10 and patients considered severe as Per RANSON score had no complications.[82]

Contrary to expectation, pseudocysts were observed in 3 patients whose APACHEII scores on admission were less than 5.These patients presented to the hospital later than 48 hours after the onset of symptoms by which time the severity of the attack may have subsided and the recorded scores were spuriously low.

The sensitivity, specificity, positive predictive value and negative predictive value were comparable with other studies in prediction of severity.On admission APACHEII scores were very sensitive for prediction of major organ failure

Table 22: Comparison with other Studies[71,72,82,81]

Study	Sensitivity	Specificity	Positive predictive value	Negative Predictive value
Savio G Barreto and Jude Rodrigues 2007	56%	98%	95%	82%
Kimmo I. Halonena et al 2003	64.7%	90.7%	NA	NA
Nurullah BULBULLER 2006	89%	89%	NA	NA
Wilsonet al1989	68%	67%	40%	87%
PRESENT STUDY				
APACHE II:	100%	80%	62%	100%
RANSON :	66.7%	86.7%	33%	96%

The APACHEII system is the only system which takes into account all the major risk factors that influence outcome from disease, including the acute physiological derangements as well as patient ability to recover which may be diminished by advancing age or chronic disease. The range of APACHEII score is wide providing better spread between mild and severe attacks, because varying weights are assigned to increasingly abnormal values, rather than all or none judgements than RANSON scoring system.

CONCLUSION

The study include 50 patients with acute pancreatitis, peak incidence was in the fourth decade with alcohol accounting for 30.3% of the attacks while gallstones accounted for 40.4%.

An APACHEII score of ≥10 on admission predicted a complicated outcome in patients Peak with acute pancreatitis with a sensitivity of 100% ,specificity of 80%,positive predictive value of 62% and negative predictive value of 100% . Scores below 10 predicted an uncomplicated outcome.

On admission APACHEII score was a better predictor of systemic complications (sensitivity100%) than RANSON score(sensitivity66.7%). Patients with APACHEII scores>10 benefitted from initial ICU care with aggressive therapy aimed at disease cure and dealing with the complications.

Hence APACHEII Scoring can be used as a reliable tool in predicting the severity and prognosis than RANSON scoring in patients with Acute Pancreatitis.

SUMMARY

In our study of the 50 patients, 12(24%) patients suffered from severe acute pancreatitis of which all 12 were diagnosed with severe pancreatitis by APACHEII score while only 4 of these 8 patients were diagnosed with severe pancreatitis by RANSON score.

The complications, systemic and local were seen in patients considered to be having severe pancreatitis by APACHEII and no complications were seen in patients considered to be having severe pancreatitis by RANSON score.

The systemic complications were multiorgan failure in 3(6%), respiratory 2(4%) and renal 2(4%) .Local complications occurred in 3 patients (6%) and both had acute fluid collection.

The age range was 24-60years (mean-42years) and sex comparision was 29(58%) men and 21(42%) women.

The causes of acute pancreatitis included biliarystone 22 (44%), alcoholism 16 (32%), idiopathic 12 (24%). 10 (20%) patients were chronic smokers 13 (26%) had atleast one co-morbid disease. The common concomitant diseases were hypertension (37.5%), diabetesmellitus (25%), ischaemic heart disease(5%).

The AUC of Apache II score was 0.717 and that of Ranson was 0.667, Sensitivity of Apache II was 100% and that of Ranson66.7%, Specificity of Apache II was 80% and Ranson 86.7% ,ppv of Apache II 62% and Ranson

33%, npv of ApacheII 100% and Rason 96% respectively.

The APACHEII system is the only system which takes into account all the major risk factors that influence outcome from disease, including the acute physiological derangements as well as patient ability to recover which may be diminished by advancing age or chronic disease. The range of APACHEII score is wide providing better spread between mild and severe attacks, because varying weights are assigned to increasingly abnormal values ,rather than all or none judgements than RANSON scoring system.

The early diagnosis and precise scoring of disease severity are important goals in the initial evaluation and management of pancreatitis. Pancreatitis not only must be differentiated from a myriad of other potential diagnosis, but patients must also be stratified to identify those with severe disease and to guide appropriate therapy.

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FIGURES

Figure 1: CULLENS SIGN

Figure 2: GREYTURNER SIGN

COMPUTED TOMOGRAPHIC PICTURES OF ACUTE PANCREATITIS

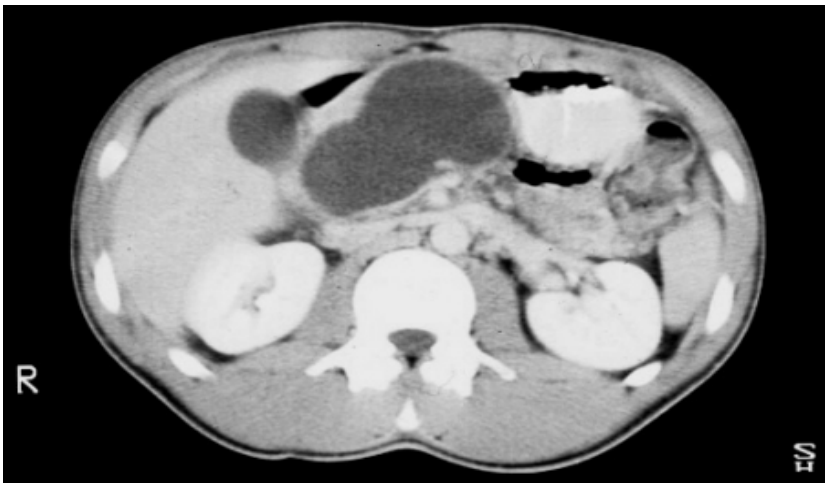

Figure 3: PANCREATIC PSEUDOCYST

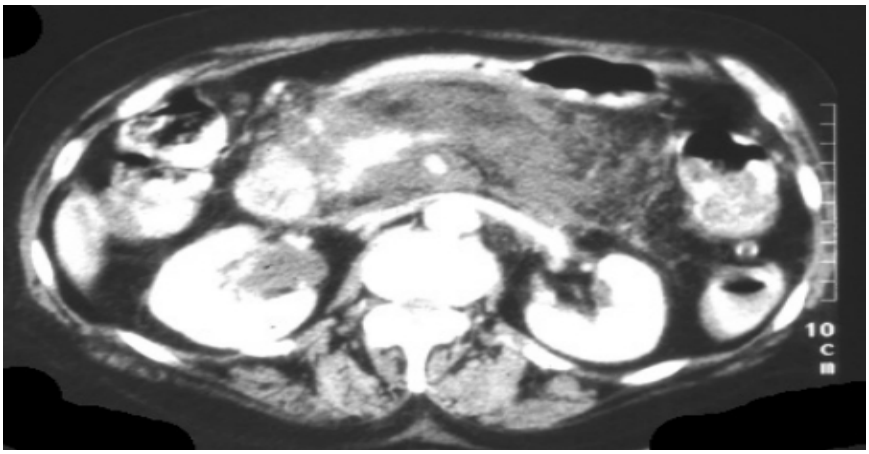

Figure 4: PANCREATIC OEDEMA AND NECROSIS

Figure 5: PANCREATIC NECROSIS

PROFORMA

PATIENT INFORMATION

NAME OF PATIENT: AGE/SEX:

HOSPITAL NO: DOA:

IP NO: DOD:

ADDRESS:

CLINICAL HISTORY:

PAIN ABDOMEN

Onset

Site & character

Radiation

Association to intake of food

Aggravating or relieving factor

NAUSEA/VOMITING

FEVER

PAST HISTORY

Gall stones

ERCP

Jaundice

Trauma/Mumps/hyperparathyroidism

Previous surgeries

Diabetes

Hypertension

PERSONAL HISTORY

Alcoholism

Drug history

Smoking history

ASSOCIATED DISEASES

GIT

CVS

RS

RENAL

IMMUNOCOMPROMISED

PHYSICAL FINDINGS ON EXAMINATION

BUILT/NOURISHMENT/HYDRATION:

Pallor Icterus Cyanosis Lymphadenopathy edema

Pulse: /min Temp: c

BP: mm of Hg Resp rate: /min

GCS:

SYSTEMIC EXAMINATION

CVS

RS

CNS

P/A

P/R

PROVISIONAL DIAGNOSIS :

INVESTIGATIONS

	At admission & Initial 48 hrs
S. Amylase	
Hb	
PCV	
TC	
SGOT	
S.Na	
S.K	
CREATININE	
RBS	
PO2	
BE	
ARTERIAL PH	
S.Ca	
BUN	

OTHER INVESTIGATIONS:

USG Abdomen

X- ray Erect Abdomen

RANSON SCORE:

At a admission or diagnosis:

Variables	Value	Scores
Age over 55		
White blood cell count over 16,000/ml		
Blood glucose level over 200mg/dl		
Serum LDH>350IU/L		
SGOT>250 Sigma Frankel Units/dl		

Initial 48 hrs:

Variables	Value	Scores
Haematocrit decrease >10%		
BUN> 5mg/dl		
Serum calcium level <8mg/dl		
Base deficit >4meq/1		
Arterial po2>60 mm hg		
Estimated fluid sequestration >6000ml		

APACHE 2 SCORING WORK SHEET

Variables	At admission	
	Value	Scores
Temp C		
MAP mm Hg 2/3 DP+ 1/3 SP		
Pulse/min		
RR/min		
Oxygenation mm Hg		
pH		
Na mmol/L		
K mmol/L		
Sr. Creatinine mg/100ml		
Haematocrit		
TC 1000/cumm		
GCS15-GCS		
TOTAL		
+ AGE POINTS		
+AGE POINTS		
+ CHRONIC HEALTH POINTS		
TOTAL APACHE II SCORE		

OUTCOME OF APACHE II SCORING SYSTEM:

OUT COME OF RANSON SCORING SYSTEM:

FINAL OUTCOME OF PATIENT:

CONCLUSION:

RANSON SCORE:[79,82]

At admission or diagnosis:

Variables	Value	Scores
Age over 55		1
White blood cell count over 16,000/ml		1
Blood glucose level over 200mg/dl		1
Serum LDH>350IU/L		1
SGOT>250 Sigma Frankel Units/dl		1

Initial 48hrs:

Variables	Value	Scores
Haematocrit decrease >10%		1
BUN> 5mg/dl		1
Serum calcium level <8mg/dl		1
Base deficit >4meq/1		1
Arterial po2>60 mm hg		1
Estimated fluid sequestration >6000ml		1

Maximum Score: 11

SCORE	Mortality rate
<3	0.9%
3-4	18%
5-6	50%
>6	90%

THE APACHE II SCORING SYSTEM 79,82

A. Age in years

Under 44-0 Points

45-54-2 points

55-64-3 Points

65-745- 5 Points

Over 74- 6 Points

Point Value for Age

B. History of severe organ insufficiency or immunocompromised?

Yes, and non- operative or emergency post – operative patient- 5 points.

Yes, and elective post – operative patient – 2 points

No- 0 points

Point Value for History

1.Rectal Temperature (Celsius)

- Over 40.9---------- 4 Points
- 39-40.9---------- 3 Points
- 38.5-38.9---------- 1 Points
- 36-38.4---------- 0 Points
- 34-35.9---------- 1 Points
- 32-33.9---------- 2 Points
- 30-31.9---------- 3 Points

Below 30, 4 points

2. Mean arterial pressure (mm Hg)

- Over 159---------- 4 Points
- 130-159---------- 3 points
- 110-129---------- 2 Points
- 70-109---------- 0 Points
- 50-69---------- 2 Points
- below 50 ---------- 4 Points

3. Heart rate

- (ventricular response)
- Over 179---------- 4 Points
- 140-179---------- 3 Points
- 110-139---------- 2 Points
- 70-109---------- 0 Points
- 55-69---------- 2 Points
- 40-54---------- 3 Points
- below 40 ---------- 4 Points

4. Respiratory rate (non- ventilated or ventilated)

- Over 49---------- 4 Points
- 35-49---------- 3 Points
- 25-34---------- 1 Points
- 12-24---------- 0 Points
- 10-11---------- 1 Points
- 6-9---------- 2 Points
- below 6 ---------- 4 Points

Point Respiratory rate

5. Arterial pH

- Over 7.69---------- 4 Points
- 7.60- 7.69---------- 3 Points
- 7.50- 7.59---------- 1 Points
- 7.33- 7.49 ---------- 0 Points
- 7.25 – 7.32---------- 2 Points
- 7.15 – 7.24 ---------- 3 Points
- Below 7.15 ---------- 4 Points

Point Value for pH

6. Serum sodium (mMol/L)

- Over 179 ---------- 4 Points
- 160-179----------3 Points
- 155- 159---------- 2 Points
- 150-154----------1 Points
- 130-149---------- 0 Points
- 120-129 ---------- 2 Points
- 111- 119 ---------- 3 Points
- Below 111---------- 4 Points

Point value Sodium Level

7. Serum potassium (mMol/L)

- Over 6.9 ---------- 4 Points
- 6.69---------- 3 Points
- 5.5- 5.9 ---------- 1 Points
- 3.5 – 5.4 ---------- 0 Points
- 3-3.4 ---------- 1 Points
- 2.5 – 2.9 ----------2 Points
- Below 2.5 ----------4 Points

Point value for K level

8. Serum Creatinine (mg/100mL)

- Over 3.4 & acute renal fail ---------- 8 Points
- 2.0- 3.4 & acute renal fail ---------- 6 Points
- Over 3.4 & chronic renal fail ---------- 4 points
- 1.5 – 1.9 & acute renal fail---------- 4 Points
- 2.0 – 3.4 and chronic ---------- ------- 3 points
- 1.5- 1.9 and chronic ---------- 2 Points
- 0.6 – 1.4 ---------- 0 Points
- Below 0.6 ---------- ---------- 2 Points

9. Hematocrit (%)

- Over 59.9 ---------- 4 Points
- 50- 59.9 ---------- 2 Points
- 46- 49.9 ---------- 1 Points
- 30-45.9 ---------- 0 Points
- 20- 29.9 ---------- 2 Points
- below 20 ---------- 4 Points

Point Value for Hematocrit

10. White blood count (total/cubic mm in 1000's)

- Over 39 ---------- 4 Points
- 20-39.9 ---------- 2 Points
- 15- 19.9 ---------- 1 Points
- 30- 14.9 ---------- 0 Points
- 1.0 – 2.9 ---------- 2 Points
- below 1.0 ---------- 4 Points

Point Value for WBC

11. Oxygenation

(Use PaO2 if FiO2 <50 %, otherwise use A -a gradient)

A- a gradient over 499 - ---------- 4 Points

A- a gradient 350-499 ---------- 3 Points

A- a gradient 200-349 ---------- 2 Point

A- a below 200 (if Fio 2 over 49 %) or

Po2 more than 70 (f Fio 2 less than 50%) ---------- 0 Points

pO2 = 61-70 ---------- 1 Points

pO2 = 55-60 ---------- 3 Points

PO2 below 55 ---------- 4 Points

Point Value for Oxygenation

12. POINT VALUE FOR GLASCOW COMA SCALE:

TOTAL OF ALL POINTS APACHE II SCORE : A+B+C

SCORE	Mortality rate
0-4	4%
5-9	8%
10-14	15%
15-19	25%
20-24	40%
25-29	55%
30-34	75%
>34	85%

MASTERCHART

S.N	Age	Chronichealthstatus	Temp. ^{0}C	MAP	HRBeatspermin	RRCyclesperMin	PaO_2mmHg	ArterialPH	NaMeq/L	K Meq/L	CrMg/Dl	Hct%	WbcCells/Cumm	GCS		Age	WbcCells/Cumm	GlucoseMg/dl	LDHIU/L	ASTIU/L	Hct%	UreaMg /dl	Camg/dl	Po2 mm Hg	BasedeficitMeq/l	FluidsrequiredLitre	
1.	42	Nil	38.1	93	80	16	90	7.36	145	3.6	1.1	40	10	15		42	10	121	99	25	40	32	9.2	90	+1	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2.	50	Nil	36.2	105	76	15	93	7.38	140	4.2	1.3	38	11	15		50	11	112	129	30	38	30	8.1	93	+1.2	2.5	
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
3.	32	Nil	37.1	73	69	15	88	7.40	133	4.5	1.7	45	9	15		32	9	104	240	15	45	28	12	88	-1	2.5	
	0	0	0	0	2	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
4.	40	Nil	38	76	75	17	90	7.51	140	4.8	1.1	41	4	15		40	4	116	180	40	41	25	11.1	90	-1.2	2.5	
	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
5.	28	Nil	39	77	78	16	94	7.34	138	3.5	1.0	35	6	15		28	6	135	186	32	35	36	8	94	+2	2.5	
	0	0	3	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0
6.	35	Nil	38.1	105	86	17	96	7.38	136	4.8	1.3	39	11	15		35	11	114	154	25	39	18	10	96	+1.1	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7.	40	Nil	37.6	105	90	14	91	7.36	143	5.1	1.4	42	5	15		40	5	90	110	20	42	16	12.6	91	+1.6	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8.	55	yes	36.9	113	68	26	86	7.40	128	4.2	1.6	45	7	15		55	7	101	196	29	45	46	10.3	86	-1.4	2	
	3	5	0	2	2	1	0	0	2	0	2	0	0	0	17	1	0	0	0	0	0	1	0	0	0	0	2
9.	58	yes	38.1	118	78	16	88	7.48	135	4.1	1.5	42	11	15		58	11	210	212	66	42	30	11.1	88	-1	1.5	
	3	5	0	2	0	0	0	0	0	0	2	0	0	0	10	1	0	1	0	1	0	0	0	0	0	0	3
10.	44	Nil	39.3	93	80	17	91	7.39	142	4.6	1.3	41	15	15		47	15	140	114	41	41	31	12.2	91	+2	2.5	
	2	0	0	0	0	0	0	0	0	0	0	0	1	0	3	1	0	0	0	0	0	0	0	0	0	0	1
11.	45	yes	36.9	73	90	18	88	7.40	139	5.1	1.1	37	10	15		45	10	116	146	30	37	18	8.1	88	+1.9	2.5	
	2	5	3	0	0	0	0	0	0	0	0	0	1	0	11	1	0	0	0	0	0	0	0	0	0	0	1

MASTERCHART

S.N	Age	Chronichealthstatus	Temp. ^{0}C	MAP	HRBeatspermin	RRCyclesperMin	PaO_2mmHg	ArterialPH	NaMeq/L	K Meq/L	CrMg/Dl	Hct%	WbcCells/Cumm in1000	GCS		Age	WbcCells/Cumm in1000	GlucoseMg/dl	LDHIU/L	ASTIU/L	Hct%	UreaMg /dl	Camg/dl	Po2 mm Hg	BasedeficitMeq/l	FluidsrequiredLitre	
12.	35	Nil	38.1	105	86	17	96	7.38	136	4.8	1.3	39	11	15		35	11	114	154	25	39	18	10	96	+1.1	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13.	40	Nil	37.6	105	90	14	91	7.36	143	5.1	1.4	42	5	15		40	5	90	110	20	42	16	12.6	91	+1.6	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14.	55	yes	36.9	113	68	15	86	7.40	128	4.2	1.6	45	7	15		55	7	101	196	29	45	46	10.3	86	-1.4	2	
	3	5	0	2	2	0	0	0	2	0	2	0	0	0	16	1	0	0	0	0	0	1	0	0	0	0	2
15.	58	yes	38.1	118	78	16	88	7.48	135	4.1	1.5	42	11	15		58	11	210	212	66	42	30	11.1	88	-1	1.5	
	3	5	0	2	0	0	0	0	0	0	2	0	0	0	10	1	0	1	0	1	0	0	0	0	0	0	3
16.	44	Nil	39.3	93	80	17	91	7.39	142	4.6	1.3	41	15	15		47	15	140	114	41	41	31	12.2	91	+2	2.5	
	2	0	0	0	0	0	0	0	0	0	0	0	1	0	3	1	0	0	0	0	0	0	0	0	0	0	1
17.	45	Yes	36.9	73	90	18	88	7.40	139	5.1	1.1	37	10	15		45	10	116	146	30	37	18	8.1	88	+1.9	2.5	
	2	5	3	0	0	0	0	0	0	0	0	0	1	0	11	1	0	0	0	0	0	0	0	0	0	0	1
18.	42	Nil	38.1	93	80	16	90	7.36	145	3.6	1.1	40	10	15		42	10	121	99	25	40	32	9.2	90	+1	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
19.	50	Nil	36.2	105	76	15	93	7.38	140	4.2	1.3	38	11	15		50	11	112	129	30	38	30	8.1	93	+1.2	2.5	
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
20.	32	Nil	37.1	73	69	15	88	7.40	133	4.5	1.7	45	9	15		32	9	104	240	15	45	28	12	88	-1	2.5	
	0	0	0	0	2	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
21..	40	Nil	38	76	75	17	90	7.51	140	4.8	1.1	41	4	15		40	4	116	180	40	41	25	11.1	90	-1.2	2.5	
	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
22.	28	Nil	39	77	78	16	94	7.34	138	3.5	1.0	35	6	15		28	6	135	186	32	35	36	8	94	+2	2.5	
	0	0	3	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0

MASTERCHART

S.N	Age	Chronichealt hstatus	Temp. ^{0}C	MAP	HRBeatspermin	RRCyclesperMin	PaO_2mmHg	ArterialPH	NaMeq/L	K Meq/L	CrMg/Dl	Hct	WbcCells/C umm in1000	GCS		Age	WbcCells/	GlucoseMg/dl	LDHIU/L	ASTIU/L	Hct%	UreaMg /dl	Camg/dl	Po2 mm Hg	Basedeficit Meq/l	Fluidsrequire dLitre	
23.	35	Nil	38.1	105	86	17	96	7.38	136	4.8	1.3	39	11	15		35	11	114	154	25	39	18	10	96	+1.1	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24.	40	Nil	37.6	105	90	14	91	7.36	143	5.1	1.4	42	5	15		40	5	90	110	20	42	16	12.6	91	+1.6	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
25.	55	yes	36.9	113	68	15	86	7.40	128	4.2	1.6	45	7	15		55	7	101	196	29	45	46	10.3	86	-1.4	2	
	3	5	0	2	2	0	0	0	2	0	2	0	0	0	16	1	0	0	0	0	0	1	0	0	0	0	2
26.	58	yes	38.5	108	78	16	88	7.48	135	4.1	1	42	11	15		58	11	210	212	66	42	30	11.1	88	-1	1.5	
	3	5	1	0	0	0	0	0	0	0	0	0	0	0	9	1	0	1	0	1	0	0	0	0	0	0	3
27.	44	Nil	39.3	93	80	17	91	7.39	142	4.6	1.3	41	15	15		47	15	140	114	41	41	31	12.2	91	+2	2.5	
	2	0	0	0	0	0	0	0	0	0	0	0	1	0	3	1	0	0	0	0	0	0	0	0	0	0	1
28.	45	yesl	36.9	73	110	18	88	7.40	139	5.1	1.1	37	10	15		45	10	116	146	30	37	18	8.1	88	+1.9	2.5	
	2	5	3	0	2	0	0	0	0	0	0	0	0	0	12	1	0	0	0	0	0	0	0	0	0	0	1
29.	42	Nil	38.1	93	80	16	90	7.36	145	3.6	1.1	40	10	15		42	10	121	99	25	40	32	9.2	90	+1	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30.	50	Nil	36.2	105	76	15	93	7.38	140	4.2	1.3	38	11	15		50	11	112	129	30	38	30	8.1	93	+1.2	2.5	
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
31.	32	Nil	37.1	73	69	15	88	7.40	133	4.5	1.7	45	9	15		32	9	104	240	15	45	28	12	88	-1	2.5	
	0	0	0	0	2	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
32.	40	Nil	38	76	75	17	90	7.51	140	4.8	1.1	41	4	15		40	4	116	180	40	41	25	11.1	90	-1.2	2.5	
	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
33.	28	Nil	39	77	78	16	94	7.34	138	3.5	1.0	35	6	15		28	6	135	186	32	35	36	8	94	+2	2.5	
	0	0	3	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0
34.	55	yes	37.1	114	69	14	84	7.4	127	4.1	1.7	42	8	15		55	28	116	194	28	42	47	10.4	84	-1.4	2	
	3	5	0	2	2	0	0	0	2	0	2	0	0	0	16	1	0	0	0	0	0	1	0	0	0	0	2
35.	35	Nil	38.0	104	84	14	94	7.36	134	4.6	1.2	38	10	15		35	10	112	153	24	38	16	10	94	1.1	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

36.	32	Nil	37.2	72	67	14	86	7.4	132	4.4	1.6	43	9	15		32	9	103	235	14	43	26	11	86	-1	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
37.	44	Nil	38	92	82	15	84	7.32	144	3.4	1.0	42	10	15		44	10	116	96	24	42	30	9	84	1	2.5	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	00	00	0	0	0	0	0	0	0	0	0	0	0
38.	26	Nil	39	90	76	14	88	7.4	142	3.5	1.1	40	10	15		26	10	114	94	22	40	28	9.5	88	2	2.5	
	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
39.	57	yes	36.9	114	66	27	86	7.4	128	3.5	1.4	38	10	15		57	10	112	92	22	45	26	9.6	87	2	2.5	
	3	5	0	2	2	1	0	0	2	0	2	0	0	0	17	1	0	0	0	0	1	0	0	0	0	0	2
40.	31	Nil	37	92	69	12	81	7.2	142	3.5	1.2	43	9	15		31	11	112	92	22	43	24	9.4	86	-1	2.5	
	0	0	0	0	0	0	00	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
41.	50	Nil	36	90	68	11	83	7.4	143	3.7	1.1	42	9	15		50	12	112	90	22	44	25	9.2	84	1.2	2.0	
	2	0	0	0	0	0	0	0	00	0	0	0	0	00	0	0	0	0	0	0	0	0	0	0	0	0	0
42.	24	Nil	32	88	67	10	83	7.3	145	3.9	1.0	36	10	15		24	11	116	90	24	42	23	9.0	86	1.1	2.0	
	0	0	0	0	0	0	0	0	0	0	0	0	00	0	0	00	0	0	00	0	0	0	0	0	00	0	0
43.	41	NIL	38.1	86	69	10	84	7.2	144	4.0	1.1	43	10	15		41	12	120	90	22	40	24	9.1	82	-1	2.5	
	0	0	0	0	0	0	0	0	0	0	00	0	0	0	0	00	0	0	0	00	0	0	0	00	0	0	0
44.	50	NIL	37	84	72	12	84	7.3	144	3.8	1.2	42	8	15		50	12	118	92	24	41	22	9.5	89	1.1	2.5	
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
45.	58	yes	37.6	116	77	14	84	7.4	146	3.8	1.1	43	12	15		58	12	212	94	23	69	24	9.0	86	1.1	2.0	
	3	5	0	2	0	0	0	0	0	0	0	0	0	0	10	1	0	1	0	0	1	0	0	0	0	0	3
46.	35	nil	37.0	116	72	12	82	7.4	144	3.5	1.1	42	10	15		35	12	116	90	24	42	24	9.0	84	1.1	2.0	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
47.	40	nil	37.0	112	71	12	82	7.4	144	3.3	1.2	44	10	15		40	12	113	90	24	42	22	9.0	82	1.0	2.0	
	0	0	0	0	0	0	0	00	0	0	0	0	0	0	0	0	0	00		0	00	0	0	0	0	0	0
48.	55	yes	37.2	114	66	12	84	7.36	126	3.7	1.7	40	11	15		55	11	112	86	23	40	46	9.2	83	1.0	2.0	
	3	5	0	2	2	0	0	0	2	0	2	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	1
49.	42	nil	37.2	116	72	12	82	7.4	143	3.5	1.1	40	12	15		42	12	114	85	24	36	24	9.0	82	1.0	2.0	
	2	0	0	0	0	0	0	0	0	0	0	0	1	0	3	1	0	0	0	0	0	0	0	0	0	0	1
50.	45	yes	36	114	71	12	84	7.4	144	3.5	1.1	40	10	15		45	12	116	84	24	34	24	9.2	84	1.1	2.5	
	2	5	3	0	0	0	0	0	0	0	0	0	1	0	11	1	0	0	0	0	0	0	0	0	0	0	1